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The Pathology of Heart Disease in Pregnancy

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THE recent book by Jensen[120] gives so complete a review of the subject of cardiac disease in pregnancy that it is unnecessary to discuss the general problems here. There is, however, one aspect, the pathological one, on which insufficient data have been published, but which can provide more definite information on certain points than is at present available in the literature. Many of the statistics given by Jensen are based on clinical reports only, and, as will be shown later, the clinical diagnosis of valvular disease is subject to a number of errors. The present study is, therefore, restricted specifically to cases in which pathological proof of the lesions was obtained by autopsy.

For this purpose an analysis has been made of 813 autopsy records of patients who died during pregnancy or the puerperium in this hospital in the last 23 years. In this series there were 108 patients who showed acute or chronic lesions of the heart valves. The clinical histories of these 108 patients have been studied and correlated with the autopsy findings. In addition, for comparison with the findings in these cases, there are also

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given, in the appropriate places, the figures from two control groups:

(*a*) A series of 1,050 autopsies in general hospitals on non-pregnant women in the child-bearing age-period, 215 of whom had various types of valvular lesions in the heart. These data are extracted from a previous paper dealing with the incidence of acute and chronic endocarditis in different sexes and at different ages (Sheehan and Sutherland[230]).

(*b*) The remaining 705 autopsies in this hospital on pregnant or puerperal women who did not have any form of valvular disease.

The initial objection to a study of this kind is that all these patients had died and that the other patients with valvular disease who survived might have had a quite different distribution of valve lesions. This objection is met so far as possible by subdividing the patients into clinical groups, such as those who died of progressive decompensation, of intercurrent illnesses, or of sudden non-cardiac accidents. A comparison of this clinical grouping with the pathological or clinical evidence of the age of the lesion gives information the value of which is capable of reasonable assessment.

It must be clearly understood that this paper is only supplementary to Jensen's excellent book, and presupposes a previous knowledge of it. A number of very significant matters are deliberately avoided here because they are adequately dealt with by Jensen or because information, additional to his, cannot be obtained from the present study. Similarly, many important papers by various authors are not mentioned here as they are analysed fully by Jensen; the only papers referred to are those which have a direct bearing on the particular subjects under discussion. In addition, the general aspects of most of the subjects in this paper have been discussed in the earlier paper by the present authors, mentioned above, and are not repeated in this one. Reference may, however, be made to the recent book on heart disease in pregnancy by Bramwell and Longson[22] and to earlier books on the subject by Frey,[68] MacKenzie,[161] and MacDonald.[159] Very simple statistical tables for the evaluation of significance in relatively small series, such as the present, are given by Loewenthal and Wilson.[153]

In the present obstetric series, the 108 patients with acute or

chronic lesions of the heart valves may be divided according to the type of valve lesion into the following groups:

(*a*) 70 patients with chronic valvular disease. Many of these had recurrent lesions, but cases of ulcerative endocarditis are not included.
(*b*) 22 patients with simple acute endocarditis.
(*c*) 6 patients with ulcerative endocarditis superimposed on previously damaged valves.
(*d*) 6 patients with subacute bacterial endocarditis, usually superimposed on previously damaged valves.
(*e*) 4 patients with primary ulcerative endocarditis.

Finally, consideration is given to a few patients with miscellaneous cardiac conditions.

A few of these cases have been described previously in a paper by Cruickshank[38] but the details have been re-analysed for the present study.

CHRONIC RHEUMATIC VALVULAR DISEASE.

Though in subsequent sections the patients who have an ulcerative lesion superimposed on chronic valvular disease are considered as a special group, they are included in this section with the patients who have uncomplicated chronic valve lesions. This is necessary for certain general considerations of the subject.

The General Incidence of Chronic Rheumatic Valvular Disease in Pregnancy.

From the analysis of nearly 9,000 reported cases of heart disease in pregnancy, Jensen (p. 134) concluded that about 1.15 per cent of all obstetric patients have clinical evidence of heart disease, and that the deaths among them form 4.3 per cent of the heart cases and 51 per 100,000 obstetric patients.

The present series of cardiac cases comes from a gross total of about 235,000 obstetric patients dealt with directly or indirectly by this hospital during the 23 years under review. This total is made up from two sources:

(*a*) The patients admitted to the hospital or attended at home by the outdoor staff of the hospital. Any of these latter patients who had complications were admitted at once to the hospital. This whole group numbers about 176,000.

(*b*) The group of patients attended at home by their own doctor but, from which, those who appeared to need special treatment were transferred to this hospital. The entire group of primarily non-hospital patients consists probably of about 59,000 women. This figure is obtained by calculating the maternal mortality of the hospital to the same level as that in the remainder of Glasgow: the hospital had 2,142 deaths in the 23 years, while the City of Glasgow has about 200 deaths annually in 22,000 births.

The figure of 59,000 women not treated in hospital is only approximate, but it is probably sufficiently accurate for the present purpose.

Among the total 235,000 patients, a clinical diagnosis of cardiac disease was made in 2,350. This figure requires two corrections in order to assess the actual incidence of chronic valve lesions. First, there are a number of hypertensive or other patients who are mistakenly diagnosed as having chronic valvular disease; from the observed incidence of cases of this type in the entire series of autopsies, it appears that they probably constitute about 150 of the clinical cardiac cases. Second, as will be shown later, only about 64 per cent of cases of chronic valvular disease are recognised clinically as such in this hospital. The actual number of cases of chronic valvular disease may, therefore, be taken as $\frac{100}{64}$ of the 2,200 remaining after the first correction, i.e. 3,440 cases.

During the period under review, 192 patients were considered on clinical grounds to have died with chronic valvular disease. As, however, only a proportion of the patients were examined post mortem, this figure cannot be accepted as accurate. A better estimate can be obtained from the autopsy series; of 813 obstetric patients examined, 82 were found to have chronic rheumatic valvular lesions. Applying this incidence of 10.1 per cent to the 2,142 deaths in the hospital during the 23-year period, it appears that 216 of the patients who died had chronic valve lesions. The percentage of these who died as an apparent result of the heart disease is discussed subsequently.

It appears, therefore, that among 235,000 obstetric patients there were 3,440 with actual chronic valvular disease and that 216 of these died. Putting these figures in the same form as Jensen's: 1.5 per cent of all the obstetric patients had chronic valvular disease; the deaths among them formed 6.3 per

cent of the cardiac patients, 92 per 100,000 total obstetric patients, and 10.1 per cent of all the maternal deaths. These figures are all higher than Jensen's. Three factors may play a part in this difference. First, Jensen's figures are based on cases diagnosed clinically and on deaths which were usually not followed by autopsy, whereas the present data are calculated to show as nearly as possible the actual numbers with chronic valvular lesions. Second, his mortality in cardiac patients is calculated only on patients who died as a result of the heart lesion; the cardiac mortality in the present series, calculated on the same basis, is 3.8 per cent, which is very close to Jensen's figure. The difference of 2.5 per cent from the total mortality is caused by deaths not directly due to the cardiac disease; the figure for these cases in the present series is similar to that given by Hamilton[85] for such cases. Third, as Jensen points out (p. 121), there are great differences in the incidence of heart disease in different parts of the world, related probably to climate. The present

	Pregnant women suffering from cardiac disease	Deaths during pregnancy or puerperium
Reid[211]	528	21
Frigyesi[71]	161	23
Gilchrist[79]	95	7
McIlroy and Rendle[160]	200	5
Herrmann[101]	41	8
Petelen[201]	20	4
Hagedorn[82]	62	7
Küstner and Schoen[143]	175	11
Nelson and Eades[181]	495	23
Abraham[1]	257	10
Daron[42]	72	2
Henderson[99]	35	2
McClure[158]	69	3
Maurizio[165]	148	8
Consoli[35]	130	1
Harris[91]	100	10
Lamb[145]	110	9
Pardee[197]	48	4
Naish[178]	450	14
Bramwell and Longson[22]	350	26
Turino and Antony[246]	102	6
	3,648	204

findings are only applicable to the locality in which they were obtained.

It is not possible to assess from these figures whether the mortality from heart disease in pregnancy is higher or lower than that in patients not pregnant, since the corresponding figures for these latter are not known. The incidence of chronic valvular disease in the control series of 1,050 autopsies on non-pregnant women of child-bearing age was 169, or 16.1 per cent. These figures are, however, taken from general hospitals to which many serious cardiac cases are admitted, and there are not any reliable data as to the total number of women with heart disease among which these deaths occurred.

Jensen (p. 135) brings some evidence to show that the death-rate among cardiac patients, which used to be in the neighbourhood of about 9 per cent, is now nearer 2 per cent. This latter figure must be considered rather sanguine; the death-rate in the publications listed on the preceding page from the years 1930 to 1938 shows a mean of 5.6 per cent. These data are not included in Jensen's table XXVI.

Valves Involved.

The chronic valve lesions which are found in pregnant women show certain differences from those found in an ordinary general hospital; mainly the absence of senile changes and the rarity of syphilitic lesions. The classification of the mechanical defects which is employed here may be briefly described. It should be noted that, though a valve may be incompetent without being stenosed, every stenosed valve is inevitably incompetent. The clinical separation of cases of mitral stenosis from cases of double mitral lesions has not any clear pathological counterpart. The question of relative incompetence of valves is not considered here.

In the mitral valve there is sometimes a scarring of the cusps and chordae without any narrowing of the orifice; this produces a pure incompetence. Moderate stenosis may be due to various types of lesions.

(*a*) Most commonly, a minor degree of the same kind of diffuse lesion that causes severe stenosis; there is fibrosis and rigidity of the cusps and chordae with a moderate narrowing of the orifice.

(*b*) Diffuse sclerosis of the cusps without scarring of the chordae.

(*c*) Scarring and closing-up of one angle of the valve, apparently progressing slowly towards the healthy angle.
(*d*) Bands across an otherwise healthy valve which appear to have been produced by the fusion and organization of isolated opposing vegetations.

Much the most common lesion, however, is the well-known severe mitral stenosis of button-hole or funnel type; this is occasionally partly calcified.

The aortic valve which becomes fibrosed usually shows a pure, but only slight, incompetence due to scarring and a little rolling of the free edges of the cusps; it is rarely that retraction is sufficient to produce much mechanical disability. There may, however, be adhesion of the cusps at their adjoining angles; the resultant stenosis may be only slight but can become moderately severe.

The tricuspid valve does not often show chronic lesions in pregnant women. When these do occur there is usually only a minor incompetence, though occasionally there may be the typical stenosis to a round hole which admits one finger.

The pulmonary valve is practically never the site of chronic lesions.

The valve incidence of the chronic lesions is shown in Table I; the data from the control series of women not pregnant are included for comparison. The cases are grouped according to the age of the patients, as this factor has previously been shown to be significant. The type and severity of the individual valve lesions are considered later.

The most striking difference between the obstetric series and the control series is the great rarity of chronic tricuspid lesions in pregnancy; their incidence is about one-tenth of that in non-pregnant women. This is seen at all age groups, and accounts for most of the difference in the incidence of chronic valvular disease between the obstetric and control groups. The reason for the very low incidence is not clear.

It was pointed out in the previous paper that nearly all patients in whom old tricuspid lesions are found at autopsy have had congestive failure. The most obvious hypothesis to explain the rarity of chronic tricuspid lesions in obstetric autopsies is that most women with such a lesion die at a fairly early age and have cardiac symptoms during most of their adult life, so that they have not married; thus they are weeded out by nature without the possibility of pregnancy having arisen. This hypo-

thesis, however, does not fit the facts. The evidence on the matter is obtained from an analysis of the data in the previous paper which deal with chronic tricuspid lesions in 42 women not pregnant between 15 and 45 years old; three additional

TABLE I.

VALVE INCIDENCE OF CHRONIC LESIONS.

Age	Total autopsies	Percentage with chronic valve lesions	Number of patients with specified chronic valve lesions			
			Mitral	Aortic with mitral	Mitral with tricuspid, with or without aortic	Aortic and others
Obstetric Series.						
16 to 25	224	8.0	12	6	0	0
26 to 35	344	12.0	25	10	3	2
36 to 45	245	9.8	14	8	2	0
Total ...	813	10.1	51	24	5	2
Non-pregnant Control Series.						
16 to 25	259	17.7	18	12	13	3
26 to 35	325	15.1	21	12	15	1
36 to 45	466	15.9	41	14	14	5
Total	1,050	16.1	80	38	42	9

cases in women who died in general hospitals 2 or 3 months after delivery have also been included. Details of the obstetric history were not available in 6 of these patients; the remaining 39 fall into 3 groups:

(*a*) 13 women who died between the ages of 16 and 25 and had been ill for so long before death that the opportunity of pregnancy could scarcely arise. Actually 2 of them were married but did not have children.

(*b*) 8 women who died between the ages of 27 and 39 and whose health had been good for sufficiently long to permit pregnancy to occur, but for the fact that they did not marry.

(*c*) 18 women who died between the ages of 27 and 43 and who had been married. All of them had been in good health in their early twenties, and many for considerably longer. Among these women 5 were nulliparae, 5 had had 1 child, 4 had had 2 or 3 children, and 4 had had 4 to 10 children.

If these data are compared with those in Table 1 of the previous paper it will be seen that from the aspect of pregnancy there is not any greater tendency to the weeding-out of patients with tricuspid lesions than of patients with mitral or aortic-mitral lesions.

Pregnancy was reasonably possible to most of the patients, and in them the occurrence and frequency of pregnancy seem to have been about normal. These findings invalidate the hypothesis that the small number of deaths in obstetric patients with chronic tricuspid lesions is related to the small number of such patients who become pregnant.

In this connexion, it is of interest to note that the 5 patients with chronic tricuspid lesions in the present series of obstetric autopsies were from 29 to 43 years of age and that their parities were 1, 2, 4, 5 and 6. The common occurrence in multiparae is noted by Jensen (p. 173).

The next question is whether the severity of the tricuspid lesion or of the associated lesions of other valves has any influence on the incidence of pregnancy or of obstetric deaths. The valve lesions are classified in Table 2. This table shows that the severity of the valve lesions is much the same in patients who have been pregnant and those who have not. A peculiar point which emerges is that the patients who died in the present obstetric series had less severe tricuspid lesions than in the control series. The severity of associated lesions of mitral and aortic is roughly similar in all groups. As noted in the previous paper, mitral lesions are always present in patients with tricuspid lesions, and aortic lesions occur in over half. Jensen (p. 173) expresses some surprise at the frequent association with aortic lesions, but his data are not abnormal.

The conclusion may be drawn tentatively that a chronic tricuspid lesion, though a serious lesion which almost always leads to death from congestive failure, is not particularly dangerous during pregnancy. If the patient is well enough to become pregnant she is usually well enough to survive the pregnancy.

Literature on Chronic Tricuspid Lesions.

The finding of an incidence of chronic tricuspid lesions in only 6.1 per cent of all obstetric patients with chronic valve lesions, as compared with 25 per cent in the control series of women not pregnant from 15 to 45 years old, indicates the need for a comparison with the incidence in obstetric autopsies recorded in the literature.

TABLE 2.

SEVERITY OF VALVE LESIONS IN WOMEN WITH CHRONIC TRICUSPID DISEASE.

	13 patients incapable of pregnancy	13 nulliparae, capable of pregnancy	13 parous women	5 obstetric patients in present series
Tricuspid				
Incompetence ...	5	5	4	4
Slight stenosis ...	6	6	6	0
Moderate stenosis	2	2	3	1
Mitral				
Incompetence ...	0	1	0	0
Slight or moderate stenosis	7	4	5	1
Severe stenosis ...	6	8	8	4
Aortic				
Incompetence ...	5	3	8	1
Stenosis	1	3	2	1

Among the 355 recorded cases of chronic valve lesions in obstetric patients, which are listed in the sections on recurrent and ulcerative endocarditis, the following 23 cases of chronic tricuspid lesions occur. These give an incidence of 6.5 per cent, which is in reasonable agreement with the incidence in the present series. The incidence of 25 per cent in the control series can be accepted as correct; the evidence is given in the previous paper. The high incidence in women is discussed by Dressler and Fischer.[46]

Tricuspid Stenosis.

Bottentuit[20]
Dressler and Fischer[46]—case 14
Eisenbach[52]—case 1
French and Hicks[63]—case 178
MacDonald[159]—case 2
Walter[269]—case 32

Tricuspid Scarring and Incompetence.

Allen and Bauer[5]
Blau[17]
Bruhschwein[27] (ref. Jensen)
Duplant[47]
Eufinger[54]
French and Hicks[63]—case 183
Friedberg and Tartakower[70]—case 1
von Jaschke[114]—case 6
Jonen[123]
Katz[124]
Kelynack[129]
Müller[176]
Nacke[177]
Porak[208]
Sée[229]
Wagner[266]—case 1
Walter[269]—case 83

In addition, there are certain cases recorded in the literature but not included in the lists of cases of chronic valvular disease and, therefore, not included in these calculations of incidence: Fier[58] and a few others listed by Jensen (pp. 172 to 176).

The Accuracy of Clinical Diagnosis.

The following evidence is included to emphasize the need for care in accepting statistics based on clinical examination only. The level of the clinical diagnosis in these patients must be accepted as quite up to the normal standard in the absence of a special cardiological clinic; the examinations were made by people with sufficient post-graduate experience to be considered reasonably competent.

Table 3 shows the comparison between the chronic valve lesions diagnosed clinically and those found at autopsy. The patients are divided into (*a*) those whose hearts were decompensated or who died from cardiac disease or had superadded ulcerative lesions, and (*b*) those who did not have such conditions. The tricuspid valve is not considered, as lesions of this valve are notoriously difficult to diagnose clinically (Bramwell and Longson[22]).

It will be observed that the accuracy of clinical diagnosis was much greater in patients who had symptoms suggesting a heart condition; this is perhaps to be ascribed to the fact that these patients were examined more carefully than the others.

The lesions of individual valves are analysed in Table 4. The diagnosis is passed as correct when a stenosis was recognized as such, whatever its severity, or when a pure incompetence was recognized as being free from stenosis. Incorrect diagnosis involved mistaking stenosis for pure incompetence or *vice versa*, or those cases in which a healthy valve was diagnosed as having any chronic lesion. The group classed as unrecognized includes

those cases in which the damaged valve appeared normal on clinical examination.

The clinical diagnosis of severe mitral stenosis was clearly much more reliable than that of other lesions. As mentioned earlier, in many of the aortic lesions the scarring of the cusps was not sufficient to produce very gross mechanical insuffi-

TABLE 3.

ACCURACY OF CLINICAL DIAGNOSIS.

Actual chronic lesion	Clinical diagnosis			
Patients with decompensation or superadded ulcerative lesions or who died cardiac deaths	Murmurs not heard	Mitral regurgitation	Mitral stenosis with or without regurgitation	Mitral and aortic lesions
Aortic incompetence or stenosis	0	0	1	0
Mitral incompetence ...	1	1	1	0
Mitral incompetence and aortic incompetence ...	0	1	2	0
Mitral stenosis, slight or moderate	4	2	4	0
Mitral stenosis, severe ...	3	1	12	4
Mitral stenosis, severe, with aortic incompetence	1	1	5	1
Mitral stenosis, severe, with aortic stenosis ...	1	2	4	2
Patients dying non-cardiac deaths without decompensation, or ulcerative lesions				
Aortic incompetence or stenosis	1	0	0	0
Mitral incompetence ...	3	1	0	0
Mitral incompetence and aortic incompetence ...	3	0	0	0
Mitral stenosis, slight or moderate	3	2	2	0
Mitral stenosis, severe ...	6	2	1	1
Mitral stenosis, severe, with aortic incompetence	3	0	0	0
Mitral stenosis, severe, with aortic stenosis ...	0	0	0	0

ciency; this may account for the failure to recognize an aortic lesion in so high a proportion of cases.

Various authors (Hamilton and Kellogg[87]; Jensen, p. 137) have commented on the inaccuracy of clinical diagnosis of heart disease in pregnancy but it will be clear from the present findings that it is quite impossible to accept Fellner's[55] conclusion on clinical grounds that only one-seventh of the cases of heart disease in pregnancy are recognized clinically.

TABLE 4.

ACCURACY OF CLINICAL DIAGNOSIS.

Pathological findings	Clinical diagnosis		
	Correct	Wrong	Unrecognized
Severe mitral stenosis	30	6	14
Slight mitral stenosis	6	4	7
Mitral incompetence	3	3	7
Aortic lesions	3	5	25

CLINICAL FEATURES OF CHRONIC VALVULAR DISEASE.

The clinical course and the manner of death in patients who have chronic valvular disease form the subject of this section. From this point onwards, the consideration of patients who have ulcerative endocarditis superimposed on a chronic valve lesion is deferred to the section dealing with that particular subject. The main details about the remaining 70 patients with chronic valvular disease are shown in Table 5.

CLASSIFICATION ACCORDING TO DECOMPENSATION.

The words decompensation and congestive failure are used interchangeably in this paper to describe the syndrome of gradual cardiac failure.

The cases are classified first into three main groups according to the clinical evidence of congestive failure 2 weeks before death. Purely terminal conditions developing in the last few days of life are not included in this grouping but are considered in the classification according to the manner of death. The three groups are:

(*a*) 38 patients without any decompensation or symptoms referable to the heart.

(*b*) 18 patients with slight decompensation; they had dyspnoea on exercise but were able to carry on ordinary household work.

(*c*) 14 patients with severe decompensation; they had the usual evidences of congestive failure, they were unable to take exercise, many of them were confined to bed and several had orthopnoea.

The diagnosis of decompensation is based essentially on dyspnoea in relation to exercise. Oedema was usually present in the more severe cases. Cough or attacks of cardiac asthma

TABLE 5.

TYPE OF DEATH IN CHRONIC VALVULAR DISEASE.

Cause of death	Decompensation during pregnancy		
	Not present	Slight	Severe
Non-cardiac			
Obstetric accidents	5	2	0
Hypertensive diseases	6	0	0
Non-septic diseases	8	2	0
Septic diseases	9	0	0
Cardiac			
Acute heart failure	5	6	3
Sudden terminal decompensation ...	3	4	0
Progressive decompensation	0	0	6
Cardiac lung complications	0	2	2
Deaths under anaesthesia	0	2	3
Cerebral embolism	2	0	0

were frequent early symptoms of decompensation, haemoptysis was usually a later symptom, and auricular fibrillation was present in some of the severe cases. The relation of these symptoms to the degree of decompensation is shown in Table 6.

TABLE 6.

INCIDENCE OF ACCESSORY INDICATIONS OF DECOMPENSATION.

Degree of decompensation	Total cases	Oedema	Cough	Haemoptysis	Cardiac asthma	Auricular fibrillation
None	38	15	3	1	0	2
Slight	18	14	7	5	3	4
Severe	14	10	8	4	2	6

There is not sufficient information recorded in these cases to discuss the incidence of râles at the bases of the lungs or radiological evidence of pulmonary congestion (Brown[26]).

The 12 cases of auricular fibrillation present certain points of interest in relation to Jensen's remarks (pp. 176 to 179). The age at death was 20 to 25 in 4 cases, 26 to 30 in 6 cases, and over 30 in the other two cases; this is much younger than in those patients suffering from chronic valvular disease without fibrillation (see Table 1) or in Jensen's data. In the 6 cases of fibrillation in patients with a history of acute rheumatism, the mean duration from the first attack of rheumatism to death was 14.5 years. Infarcts were found in the kidneys in 1 case and in the spleen in 2 cases, but systemic embolism does not seem to have occurred in the other 9. Among the 58 patients without fibrillation infarcts were present in 9: in kidneys 6, in spleen 2, and in brain 2. The difference cannot be considered very important.

Time of Onset of Decompensation.

The time of onset of the decompensation is shown in Tables 7 and 8.

About half of the patients who had congestive failure in pregnancy gave a history of some dyspnoea before its onset, though never very severe; this tended to become worse in the first few weeks of pregnancy. Most of the others developed the congestive failure either in the first 12 weeks of pregnancy or at about 24 to 30 weeks and, in these, the onset was sometimes rather sudden so that the patient could date it accurately.

This occurrence in two phases is in agreement with the conclusions of Brandstrup.[23] It is not in accord with the series of cases tabulated by Jensen (p. 150), but Jensen points out that his data on this matter are inadequate. Lennie,[150] Tunis,[245] and Haupt[94] maintain that in most cases congestive failure occurs before the 6th month, though Lamb[145] and Brown[26] consider it more frequent in late pregnancy. The various theories on the matter are discussed in these papers.

Classification According to Type of Death.

The cases are also cross-classified in Table 5 according to the manner of death.

The non-cardiac deaths include those cases in which the heart lesion appears not to have been a factor of any importance in causing death.

The first group is that of accidental deaths. These patients had been in apparently perfect health until a few hours before death; they died suddenly as a result of obstetric catastrophes such as ruptured uterus, acute inversion of the uterus, or a single fatal haemorrhage due to placenta praevia. Every case in which there

TABLE 7.
TIME OF ONSET OF DECOMPENSATION.

Clinical grouping	Time of onset of decompensation				
	Before pregnancy	Weeks pregnant			
		0-12	13-23	24-30	31-40
Slight decompensation					
Cardiac death	2	5	0	7	0
Non-cardiac death	3	0	0	1	0
Severe decompensation					
Cardiac death	10	2	1	1	0

TABLE 8.
TIME OF ACCENTUATION OF DECOMPENSATION IN PATIENTS WITH MILD DEGREES BEFORE PREGNANCY.

Clinical grouping	Time of accentuation of decompensation				
	Not worse in pregnancy	Weeks pregnant			
		0-12	13-23	24-30	31-40
Slight decompensation					
Cardiac death	1	0	0	0	1
Non-cardiac death	2	0	0	1	0
Severe decompensation					
Cardiac death	0	5	2	1	2

was any evidence, clinical or pathological, to suggest toxaemia, sepsis or anaemia during the pregnancy has been excluded from this group. In the control series of patients with heart disease who were not pregnant the comparable group is that of deaths due to suicide or road accident without any prior cardiac symptoms. This group is of particular significance with regard to the question of recurrent endocarditis and is discussed in that connexion later.

The second group of non-cardiac deaths includes those

usually associated with hypertension, such as those due to eclampsia, accidental haemorrhage, or nephritis. The third group includes a variety of non-septic diseases, whether related to pregnancy or not, such as hyperemesis, anaemia or epilepsy. The fourth group consists of septic diseases such as primary pneumonia, pyelonephritis or puerperal sepsis.

The cardiac deaths may be described in more detail.

Acute heart failure. This is an extremely sudden and severe cardiac failure developing in a patient who had usually appeared to be in relatively good health a few hours before death. There was a catastrophic onset of urgent dyspnoea and cyanosis, semi-coma with great restlessness, a very weak pulse which was irregular in many cases, and adventitious sounds all over the lungs. These patients died within 1 to 12 hours after the onset of symptoms.

This condition appears to be the same as that described by Jensen as acute pulmonary oedema and is discussed later.

Sudden terminal decompensation. This is clinically a rather longer and more gradual type of heart failure than in the previous group. Most of the patients had been previously in normal health or only slightly decompensated. They suddenly developed a rapidly progressive dyspnoea and died with the typical picture of severe congestive failure, usually with auricular fibrillation. Death occurred in 2 or 3 days in most cases, though occasional patients remained alive for 10 to 12 days.

Progressive decompensation. This group includes those patients who, for several weeks before death, had serious evidence of congestive failure, becoming gradually and steadily worse until death. The course during the last day was sometimes rather rapid.

Cardiac lung complications. This refers to patients who had pulmonary infarcts which became infected, leading to empyema, pneumonia, or gangrene of the lung. It was usually associated with congestive failure; the lung complications were in the nature of unfortunate accidents but appeared to play the predominant part in the fatal issue. These cases were usually recognized only at the autopsy. It should be noted that the presence of ordinary pulmonary infarctions, such as are seen so commonly in decompensated patients, is not a sufficient basis for inclusion of a case in this group.

Death under anaesthesia. In most cases the anaesthetic was given for surgical delivery which was undertaken because the cardiac condition appeared to warrant interference. Nevertheless

it is often difficult to assess how far the anaesthetic and how far the cardiac condition were responsible for death.

Cerebral embolism. This occasionally occurred in patients almost without evidence of previous cardiac disease. It sometimes occurred during anaesthesia; the patient never became conscious after the anaesthetic and died a day or two later. This may be related to the changes in cerebral circulation under anaesthesia. This subject is discussed in detail by Jensen (pp. 218 to 224).

The Cause of Decompensation.

The present analysis deals only with the data which are obtained from the clinical and pathological findings in the cases studied. It does not include a consideration of the various functional disturbances which may lead to congestive failure in patients who are not pregnant nor of the circulatory changes which occur in pregnancy. These matters are amply discussed by other authors and are summarized by Jensen (pp. 17 to 96).

The first point that is clear from the present series is that there is a definite relation between the mechanical severity of the stenosis of valves and the tendency for the patient to become decompensated.

The Severity of Valve Lesions.

Table 9 shows the valve lesions classified according to the manner of death. It is, of course, not possible from the present data to estimate the death-rate among patients with each type of valve lesion, since the only source of information as to the total number of live patients with each lesion is clinical and, therefore, not reliable. But conclusions as to the relative importance of the different lesions can be drawn from the manner of death, whether non-cardiac or cardiac. It will be seen from the table that there is a very definite relation between the severity of the valve lesion and the tendency to decompensation or to die a cardiac death.

As noted earlier, the aortic incompetence is usually only of a minor grade; it does not appear to influence the type of death.

Mitral incompetence, with or without aortic incompetence, is the least important lesion; only 36 per cent of the patients had any evidence of congestive failure or died cardiac deaths.

Mitral stenosis of slight or moderate grade is rather more important; 46 per cent of the patients had congestive failure or died cardiac deaths.

Severe mitral stenosis, with or without aortic incompetence, is more serious still; 64 per cent of the patients had congestive failure or died cardiac deaths.

Severe mitral stenosis associated with aortic stenosis appears to be the worst lesion; 100 per cent of the patients had congestive failure or died cardiac deaths.

TABLE 9.

RELATION OF CHRONIC VALVE LESIONS TO DECOMPENSATION.

(T indicates that one of the number had a chronic tricuspid lesion.)

	Not decompensated		Slight decompensation		Severe decompensation
	Non-cardiac death	Cardiac death	Non-cardiac death	Cardiac death	Cardiac death
Aortic incompetence ...	1	0	0	0	0
Mitral incompetence ...	4	2	0	1	0
Mitral incompetence with aortic incompetence ...	3	0	0	1	0
Mitral, slight or moderate stenosis ...	7T	2	2	1	1
Mitral, severe stenosis ...	10T	3	1	5	8T
Mitral, severe stenosis with aortic incompetence	3	1	1	2	2T
Mitral, severe stenosis with aortic stenosis ...	0	2	0	3	3T
Aortic stenosis	0	0	0	1	0

It is rather difficult to assess the effect of the few tricuspid lesions; only one patient had a tricuspid stenosis (the case with mitral stenosis and aortic incompetence) and all the cases were associated with relatively serious mitral lesions. Severe decompensation occurred in 60 per cent.

In the modern literature there is a tendency to consider that the type and severity of the valve lesion are not of great significance and that the important question is the condition of the myocardium (Hunt[109]; Fr. Jensen[119]). These views are usually based on clinical considerations. It is to be remembered, however, that it is very difficult to assess the mechanical severity of a valve lesion by clinical examination. The pathological findings in the present series indicate that the views of the earlier writers on this subject are more in keeping with the facts; the type and

severity of the valve lesion are matters of very definite importance in the question of whether the heart of the patient is liable to become decompensated. Of recent years this view has been gaining ground again (Lamb[145]; von Jaschke[117]; Oppel[188]). Jensen (pp. 163 to 176) discusses the relative importance of various valve lesions. He recognizes the possible fallacies of clinical diagnosis but concludes from the available evidence that mitral stenosis has an unfavourable prognosis, particularly when it is combined with an aortic lesion. He is, however, doubtful of the significance of tricuspid lesions.

It is of interest that the valve lesions which lead to acute heart failure or terminal decompensation are not significantly different from those in other kinds of death. This is seen from Table 10. Jensen's conclusions on this matter (p. 232) are very tentative; he suspects that combined aortic and mitral lesions may predispose to acute heart failure.

TABLE 10.

RELATION OF CHRONIC VALVE LESIONS TO RAPID CARDIAC DEATHS.

Valve lesion	Acute heart failure	Terminal decompensation
Mitral incompetence	1	1
Mitral, slight or moderate stenosis	3	0
Mitral, severe stenosis	7	3
Mitral, severe stenosis with aortic incompetence	0	1
Mitral, severe stenosis with aortic stenosis	2	2
Aortic stenosis	1	0

The problem remains of why one patient should develop congestive failure while a patient with an apparently identical valvular lesion does not. The same problem applies to the individual: a patient whose heart decompensates has presumably had a valvular lesion of about the same degree of severity for a long time before the decompensation began. The valvular lesion is, therefore, only one of the factors leading to decompensation, and a number of other possible factors need consideration.

Heart Weight.

It has been considered by some authors that the degree of hypertrophy of the heart may be one of the controlling factors

in the aetiology of congestive failure. Certainly a patient with normal heart valves, who has a chronic hypertension with hypertrophy of the left ventricle, is liable to develop evidence of congestive failure in the later stages of the disease, and particularly when pregnancy occurs. But there is not any convincing evidence in the present series of patients with chronic valvular disease to indicate that congestive failure is more liable to occur in patients with much hypertrophy of the heart than in those with little. The mean heart-weights in the present series are shown in Table II, excluding one *cor bovinum* due to gross aortic stenosis.

TABLE II.

RELATION OF HEART WEIGHT TO DECOMPENSATION.

	Heart weight, gm.	
	Mean	Range
Not decompensated		
Non-cardiac death	350	250 to 510
Cardiac death	400	310 to 530
Slight decompensation		
Non-cardiac death	380	280 to 550
Cardiac death	380	240 to 570
Severe decompensation		
Cardiac death	390	280 to 640
Normal heart in pregnancy	280	240 to 320

The weight of the heart does not seem to be a deciding factor in the aetiology of acute heart failure; the mean weight of the heart in such cases was 380 gm. with a range of 240 to 640 gm.

Jensen (pp. 160 to 162) summarizes the clinical evidence on this subject and concludes that there is some relation between the size of the heart and the tendency to decompensation. The present data cannot be considered to support this view.

In this connexion, it may be noted that hypertension related to pregnancy does not appear to play any important part in precipitating congestive failure in a patient with a chronic valve lesion.

Lung Weight.

Cases of the type which is classified here as acute heart failure have been recorded as acute pulmonary oedema in many articles in the literature, and are discussed under this heading

by Jensen (pp. 224 to 233). The term "acute pulmonary oedema" is, however, not a very satisfactory one.

In patients without cardiac disease the typical clinical picture of acute pulmonary oedema is sometimes substantiated at the autopsy by the finding of gross oedema of the lungs, but in a not inconsiderable number of cases the lungs are found to be almost dry.

In patients with cardiac disease, on the other hand, the clinical diagnosis of pulmonary oedema is practically never disproved by the pathologist. The reason is that almost every patient who dies with chronic valvular disease has some degree of pulmonary oedema at autopsy, whatever the manner of death. Acute heart failure is certainly accompanied in many cases by a rather more severe oedema of the lungs at autopsy than is usually found in patients with cardiac disease who have died in other ways, but the differences are not very striking. The weights of the lungs in the three types of death in patients with chronic valvular disease are shown in Table 12; patients with gross pneumonia or large pulmonary infarcts are excluded. It would appear that the view that acute pulmonary oedema is the cause of a specific type of cardiac death does not rest on a satisfactory basis.

TABLE 12.

RELATION OF LUNG WEIGHT TO DECOMPENSATION.

Type of death	Weight of both lungs together, gm.	
	Mean	Range
Acute heart failure	1340	680 to 1640
Other decompensation or cardiac deaths	1110	790 to 1590
Not decompensated, non-cardiac deaths	1090	460 to 1820
Normal lungs without congestion or oedema	420	360 to 520

Other Pathological Changes in the Heart.

The last question is whether the decompensation is the result of an acute myocarditis or of an acute endocarditis. This subject is a very big one and is discussed in the following section on Recurrent Endocarditis.

Obstetric Factors.

Relation to Delivery.

The matter of most interest in this connexion is the relation of death to delivery. A patient with cardiac disease is usually treated in the later stages of pregnancy as a person unfit to take exercise. She then has to undergo the great physical task of labour and delivery. In theory it would be expected that her heart would become severely decompensated or that she would die either during labour or within a few hours afterwards. In practice this is not usually the case.

Table 13 shows the time of death in relation to delivery in the various types of patients with cardiac disease and in the control series of obstetric patients without cardiac disease. It

Table 13.

Time of Death in Relation to Delivery.

	Time of death						
			After delivery				
	During pregnancy	During labour	0 to 4 hours	5 to 24 hours	1 to 4 days	5 to 10 days	Over 10 days
Not decompensated							
Non-cardiac death ...	3	1	4	5	3	6	6
Cardiac death ...	2	0	1	1	3	2	1
Slight decompensation							
Non-cardiac death ...	0	1	0	1	0	2	0
Cardiac death ...	5	2	3	0	0	0	4
Severe decompensation							
Cardiac death ...	2	1	2	2	1	2	4
Control obstetric patients without any valve lesions ...	71	56	155	141	70	143	69

will be seen that the deaths during labour or the first day after delivery are relatively rather less frequent among the patients with heart disease than among the controls. This is particularly the case with regard to the cardiac deaths. This general conclusion, however, requires some critical analysis, mainly with regard to three points:

(*a*) The control series is not a completely fair standard of

comparison. Most of the deaths among the patients with normal hearts result from acute obstetrical conditions and these deaths, therefore, tend to occur during labour or shortly afterwards. The women with chronic valve lesions, on the other hand, have been in many cases hospital patients during the last weeks of pregnancy; the deaths among these antenatal cases are naturally commoner than in patients without cardiac disease. This accounts to some extent for the greater number of cardiac deaths in the antenatal period than would be expected from the control series.

(*b*) A more detailed grouping of the cardiac deaths is shown in Table 14. From this it will be seen that most of the deaths

TABLE 14.

CARDIAC DEATHS IN RELATION TO DELIVERY.

	Time of death						
			After delivery				
Type of death	During pregnancy	During labour	0 to 4 hours	5 to 24 hours	1 to 4 days	5 to 10 days	Over 10 days
Acute heart failure ...	4	1	3	2	2	1	1
Anaesthesia	0	2	2	0	0	0	1
Terminal decompensation ...	3	0	0	1	0	1	2
Progressive decompensation ...	1	0	1	0	1	1	2
Cardiac lung complications ...	1	0	0	0	0	1	2
Cerebral embolism ...	0	0	0	0	1	0	1

during labour or the first day after delivery are due to acute heart failure, or occur under anaesthesia. The patients with progressive or terminal decompensation do not tend to die at this time.

The relative frequency of deaths due to acute heart failure at this time raises the question of when the acute failure actually began. This is shown in Table 15, from which it will be seen that 3 of these deaths were due to an acute failure, the onset of which was during labour (1 in the 1st stage and 2 in the 2nd stage). The fourth case had the onset very shortly before labour and the remaining 2 cases within a few hours after delivery.

This table indicates also that the tendency to acute failure during labour is not related to the degree of decompensation previously.

TABLE 15.

TIME OF ONSET OF ACUTE HEART FAILURE IN RELATION TO DELIVERY.

Degree of decompensation	Time of onset of acute heart failure						
			After delivery				
	During pregnancy	During labour	0 to 4 hours	5 to 24 hours	1 to 4 days	5 to 10 days	Over 10 days
None	1	1	0	0	2	1	0
Slight	3	2	0	0	0	0	1
Severe	1	0	1	1	0	0	0

Jensen (p. 229) concludes that two-thirds of all the cases of acute heart failure occur as a complication of congestive failure and that the other third occur without such an association. This is in agreement with the present figures of 9 and 5 in the two groups as shown in Table 5. From a study of 135 patients with regard to the time of delivery, he concludes (p. 230) that death from acute heart failure during or immediately after labour is less common in the decompensated than in the non-decompensated patients. The present figures are not sufficiently numerous for any deductions on this point.

Thus the cardiac deaths during labour or soon after delivery cannot be ascribed to the progressive exhaustion of a badly decompensated heart during the physical strain of labour; they are usually catastrophic failures in patients who have been either not or only slightly decompensated.

(*c*) Another method of considering this problem is to calculate the absolute death-rate at various times in relation to delivery in patients with or without valve lesions.

It was shown earlier that the gross death-rate in the present series of patients suffering from chronic valvular lesions was 6.3 per cent as compared with 0.9 per cent in the control series of patients without valve lesions. Applying these figures to the data of Table 13, it is an easy calculation to find the death-rate at various times in relation to delivery. In this particular paragraph it is necessary to include also the 12 patients who had

ulcerative or subacute bacterial endocarditis superimposed on the chronic lesion, as they are also included in the calculations of gross death-rates; they are grouped in Table 16 with the cardiac deaths. For comparison, the data of Jensen are given; these are calculated from his collected figures on p. 153 and from his death-rate from cardiac causes of 4.3 per cent of patients with chronic valvular disease.

It will be seen from Table 16 that the present findings for cardiac deaths agree reasonably with those of Jensen.

TABLE 16.

RELATION OF TYPE OF DEATH TO DELIVERY.

	Time of death				
			After delivery		
	During pregnancy	During labour	First 24 hours	1 to 4 days	5 to 28 days
JENSEN'S DATA					
Cardiac deaths in 10,000 obstetric patients with chronic valve lesions	68	40	75	71	131
PRESENT DATA					
Deaths in 10,000 obstetric patients with chronic valve lesions:					
Cardiac deaths	92	38	77	46	131
Non-cardiac deaths	23	15	77	23	108
PRESENT DATA					
Non-cardiac deaths in 10,000 *control* obstetric patients with normal valves	9	7	38	9	27

During pregnancy, labour, or after the first day of the puerperium the cardiac deaths are from 5 to 9 times as many as the controls. During the first day of the puerperium such deaths are absolutely the most frequent, though relatively they are only twice as many as the controls. It must be emphasized that the cardiac deaths do not include deaths from the ordinary obstetric complications. In the control series, on the other hand, all the patients die from obstetric or other medical complications; there are not any deaths from heart disease. For a true comparison of the deaths in the control series it is necessary to take the group of deaths not due to the heart condition in patients with chronic

valve lesions. The table shows that these non-cardiac deaths are twice as common as in the controls during pregnancy, labour, or the early puerperium, and four times commoner in the late puerperium. This illustrates the bad influence of even a symptomless valve lesion on the ordinary obstetric complications. It is of interest to note from this table that the statistics do not bear out the common statement that one of the most dangerous times for the patient with chronic valvular disease is about the third day after delivery.

TABLE 17.

RELATION OF DECOMPENSATION TO DURATION OF PREGNANCY.

	Duration of pregnancy in weeks			
	To 19	20 to 29	30 to 35	36 and over
Not decompensated				
Non-cardiac death	2	1	8	17
Cardiac death	1	1	1	7
Slight decompensation				
Non-cardiac death	0	0	1	3
Cardiac death	0	1	5	8
Severe decompensation				
Cardiac death	0	3	6	5
Control obstetric patients without any valve lesions	56	42	106	501

Duration of Pregnancy.

Table 17 shows that there is some tendency for patients with decompensated hearts to die or be delivered before the last month of pregnancy. This is not due to the inclusion of patients in whom the pregnancy was terminated artificially; the only inductions of labour before 36 weeks were in 2 patients whose hearts were not decompensated and whose deaths were not due to the condition of their hearts; these were at 17 and 34 weeks respectively. Jensen (p. 199) considers that the higher incidence of premature labour in patients with cardiac disease is probably related to congestive failure.

The tendency to prematurity and thus to easier delivery in patients with cardiac disease in general might be considered a factor in reducing the mortality in labour and in the few hours after delivery. Actually there is not any relatively greater mortality at that time in women who are at or near full-time than

in women who are only 6 to 7 months pregnant. This is seen in Table 18 which shows the data from the patients whose hearts were decompensated or who died cardiac deaths.

TABLE 18.

RELATION OF TIME OF CARDIAC DEATH TO DURATION OF PREGNANCY.

Time of death	Duration of pregnancy in weeks		
	To 29	30 to 35	36 and over
During pregnancy	2	4	3
During labour or within 4 hours after ...	1	3	6
During puerperium	3	6	14

Age.

As shown in Table 19 the age of the patient does not appear to have much influence on the question of decompensation. The

TABLE 19.

RELATION OF AGE TO DECOMPENSATION.

	Age		
	16 to 25	26 to 35	36 to 45
Not decompensated			
Non-cardiac death	3	15	10
Cardiac death	2	3	5
Slight decompensation			
Non-cardiac death	0	1	3
Cardiac death	3	10	1
Severe decompensation			
Cardiac death	4	8	2
Control obstetric patients without any valve lesions	190	303	212

increase in the death-rate among the older patients is chiefly due to the greater number of deaths in the non-decompensated group. Jensen (p. 159) does not consider that it is a phenomenon specifically related to pregnancy. Fr. Jensen[119] considers that the longer the heart disease has lasted the more dangerous do pregnancy and parturition become, owing to a progressive fibrosis of the myocardium, but this view appears to be quite speculative.

Parity.

Table 20 shows that there is not any relation between the parity of the patient with a chronic valve lesion and the tendency of her heart to decompensate.

TABLE 20.

RELATION OF PARITY TO DECOMPENSATION.

Decompensation	Parity 1	2 and 3	4 and over
None			
Non-cardiac death	10	6	12
Cardiac death	3	3	4
Slight			
Non-cardiac death	0	1	3
Cardiac death	10	2	2
Severe			
Cardiac death	6	3	5
Control obstetric patients without any valve lesions	282	169	254

There is, however, one very definite relation of decompensation to multiparity. A patient may pass through many pregnancies without her heart becoming decompensated; but, if this condition occurs in any pregnancy, she very rarely passes through a subsequent pregnancy without her heart again becoming decompensated (Jensen, p. 184). Nelius[180] is one of the rare authors who disagree with this.

The details about multiparae in the present series are as follows:

(*a*) 20 patients who died without decompensation in the final pregnancy, had had from 1 to 9 previous pregnancies (mean 3.3) but had not been decompensated in any of them.

(*b*) 6 patients who had slight or severe decompensation in the final pregnancy, had not been decompensated in any of the previous pregnancies which were from 1 to 6 in number (mean 2.7).

(*c*) 7 patients who had had slight or severe decompensation in the final pregnancy, had first of all had 0 to 7 pregnancies (mean 3.7) without decompensation and then a series of 1 to 5 pregnancies (mean 2.2) with decompensation in all of them.

(*d*) 2 patients gave less typical histories. One had slight symptoms suggesting congestive failure in her first pregnancy, had 2 subsequent pregnancies without decompensation, and became slightly decompensated in her last pregnancy. The other had 7 pregnancies without decompensation, was decompensated in her 8th, had a 4-months miscarriage in her next pregnancy without any decompensation, and was slightly decompensated in her last pregnancy. In this case it is probable that the 9th pregnancy was not sufficiently advanced for decompensation to develop.

The previous clinical histories in the present series are not sufficiently detailed for any conclusions as to whether the decompensation in subsequent pregnancies tended to begin earlier than in the previous pregnancies.

The American Heart Association Classification.

The classification of the American Heart Association (Jensen, pp. 140 to 142) merits a few remarks. This functional classification has been applied to cardiac disease in pregnancy by numerous authors (Pardee,[195] Herrmann and King,[102] Reid,[211] Eastman,[50] MacLennan,[162] Adair and Stieglitz,[2] Hanley and Anderson,[89] Daichman and Kornfeld,[40] McClure,[155] Stander,[236] Stander and Kuder,[237] Oppel[188]). At first glance it has an attractive simplicity. The patients are allocated into 4 grades according to the degree of decompensation; Grade I consists of patients without any decompensation, Grade II*a* what has been called slight decompensation in the present paper, Grades II*b* and III are the lesser and greater degrees of the condition referred to in this paper as severe decompensation. Various workers maintain that the prognosis can be estimated satisfactorily from the grade at which the patient is assessed.

The difficulty lies in the time of pregnancy at which the assessment is made. Decompensation may begin at various stages of pregnancy and may progress at various rates. In the American Heart Classification nearly all workers appear to grade their patients at the time they are first seen at the hospital, though only a few give a definite statement to this effect (Gilchrist,[79] McIlroy and Rendle,[160] Naish,[178] Pardee[197]). Such a time is obviously quite fortuitous. It is recognized by some authors that reclassification may be required as pregnancy

advances (Lamb,[144] Pardee,[196] Fitzgerald,[60] and Bramwell and Longson[22]) and for this reason Bramwell and Longson classify their patients before pregnancy begins.

In the present paper the degree of decompensation has been assessed at a given short time before death. This is satisfactory for a series of dead patients, but it is obviously inapplicable in clinical work. For that purpose it is necessary to consider the prognosis at a given stage of pregnancy. In Table 21 the present series of patients is subdivided into those with and those without any evidence of decompensation at specific times of pregnancy. It will be seen that, irrespective of the time at which the decompensation first appears, a patient whose heart is decompensated in pregnancy is very much more liable to die a cardiac than a non-cardiac death. This is so well known in ordinary practice as hardly to need statistical proof. But, a consideration of all

TABLE 21.

RELATION OF DECOMPENSATION AT VARIOUS STAGES OF PREGNANCY TO SUBSEQUENT CARDIAC DEATH.

	Total patients alive at this stage of pregnancy	Cardiac death later in pregnancy or puerperium
Any decompensation		
Before pregnancy	15	12
At 12 weeks	22	19
At 23 weeks	22	19
At 30 weeks	27	23
At 35 weeks	16	13
Not decompensated		
Before pregnancy	55	26
At 12 weeks	48	19
At 23 weeks	42	16
At 30 weeks	31	7
At 35 weeks	24	7

patients with chronic valvular disease, who die from any cause during pregnancy or the puerperium, shows that over a third of those whose hearts are not decompensated at all at 23 weeks are destined to die a cardiac death.

This analysis of the present series shows one of the chief deficiencies of the American Heart Classification as it is usually applied. If the present series had been assessed according to

that classification at 23 weeks, two-thirds of the patients would have been allocated to Grade I which is reputed to have a negligible mortality. As a result, nearly half of the subsequent cardiac deaths would have been in patients to whom an excellent prognosis had been given. On the other hand, at 30 weeks, over half the patients would have been allocated to Grade I but only a quarter of the cardiac deaths would have been unforeseen.

The American Heart Classification is thus of some significance when it is based on the patient's condition in the last quarter of pregnancy, but it is of relatively little value before the middle of pregnancy. This aspect does not appear to have been sufficiently stressed in the literature. The shortcomings of the system have led various workers (Hamilton[83, 84, 86], Newell,[184] C. Young,[281] Carr and Hamilton,[32] Schuman,[226] Lamb,[145] Carr,[31] Blumenfeld[18]) to group all patients with definite valvular disease into one single class in which they usually do not attempt sectional prognosis except for the general principle that a patient whose heart is seriously decompensated is more likely to die of her heart disease than a patient with a symptomless valve lesion. Most of these authors do, however, separate off into different groups the patients who have cardiac neuroses or functional cardiac conditions without a pathological valve lesion. In these groups the prognosis is, of course, excellent.

RECURRENT ENDOCARDITIS.

In many of the cases with chronic rheumatic valvular disease, fresh vegetations which are apparently of simple type are found at autopsy. These are referred to here as recurrent vegetations. They usually affect the scarred valves, but sometimes are found also on previously undamaged valves. They are warty in appearance, and vary in height from 1 to 4 mm.; there is a definite tendency for them to be larger in pregnant women than in other patients. They occur sometimes as a fairly continuous vegetation along the contact line of the valve, but more usually as isolated masses which may lie in corresponding pairs on opposite sides of the valve or which may occupy one angle of a scarred valve. In many cases the valve is so rigid that it is difficult to imagine that the segments have had any actual contact at the site of the vegetations. Histologically the vegetations have the ordinary structure of the simple non-ulcerative variety, and do not show any bacteria.

Details were given in the previous paper about the relations of recurrent endocarditis in patients not pregnant to various factors, such as age, sex, and type of death. It was shown that recurrent endocarditis is probably of rare occurrence in the patient who is not pregnant and who is apparently in good health apart from symptomless chronic valvular disease. It was also noted that its incidence is affected by four factors: (*a*) it is common in young patients but shows a decreasing incidence with age; (*b*) it is commoner in decompensated patients than in those not decompensated; (*c*) it is sometimes found in patients who die of intercurrent illnesses; (*d*) it is relatively uncommon on calcified valves.

The present data show another factor; any patient with chronic rheumatic valvular disease who becomes pregnant is very liable to develop recurrent endocarditis without any recognizable exciting cause other than the pregnancy itself.

Incidence in Pregnancy.

Table 22 shows the findings in the present series of obstetric patients compared with those in the control series of non-pregnant women. (Three of the cases with chronic valve lesions, 2 M and 1 MT, are excluded from consideration in this section as a satisfactory investigation was not made at these autopsies as to whether any recurrent vegetations were present or not.) It will be seen from the table that there is a very much higher incidence of recurrent endocarditis in the obstetric series than in the controls; 79 per cent as compared with 51 per cent. The incidence in both groups shows a gradual fall with advancing age, either when the cases are taken all together or when they are subdivided according to the manner of death, but the proportion is always higher in the obstetric patients.

The classification according to type of death is based on the details in the previous section. The patients grouped under the heading of accidental death are of particular interest. They may be taken as a fair sample of the condition, during life, of patients with symptomless old valvular disease which is uncomplicated by other factors. From a pathological aspect they may be compared with experimental animals which are killed for purposes of study at various stages of a disease. The cases are too few for statistical significance but, when they are considered in association with the other data, certain interpretations seem legitimate. It appears that a non-pregnant patient with chronic

TABLE 22.

INCIDENCE OF RECURRENT ENDOCARDITIS ON CHRONIC VALVE LESIONS.

Type of death	Obstetric patients: Age groups 16 to 25	26 to 35	36 to 45	Recurrence per cent
Not decompensated. Died from obstetric accidents	1 / 1	1 / 2	0 / 1	50
Not decompensated. Died from various diseases	2 / 2	9 / 12	4 / 9	65
Any decompensation or cardiac death	9 / 9	18 / 20	9 / 11	90
Recurrence per cent	100	82	62	79

Type of death	Non-pregnant women: Age groups 16 to 25	26 to 35	36 to 45	Recurrence per cent
Not decompensated. Died from accidents	0 / 3	0 / 2	0 / 2	0
Not decompensated. Died from various diseases	2 / 5	4 / 10	6 / 23	32
Any decompensation or cardiac death or acute rheumatism	27 / 32	23 / 34	16 / 43	61
Recurrence per cent	72	59	32	51

(In the above table the upper figures in each fraction show the number of patients with recurrent endocarditis and the lower figure shows the total number with chronic lesions.)

valvular disease does not have recurrent endocarditis so long as her heart is not decompensated and she is free from complicating diseases. But, if she becomes pregnant, particularly if she is young, she is liable to develop recurrent endocarditis as a result apparently of the pregnancy itself without any other factor being present.

When other factors come into play, as in the other types of death, the effect of pregnancy is superimposed on that of the

complicating factor. The pregnant patients grouped as having died of various diseases but without congestive failure can reasonably be compared with the corresponding group in women not pregnant, as many of the diseases are similar. The incidence of recurrence is clearly higher in the obstetric patients.

Nearly all of the obstetric patients whose hearts had been decompensated or who had died cardiac deaths had recurrent endocarditis. This is even more striking when the patients with calcified valves are excluded; as mentioned above, calcification of a valve renders it much less liable to recurrent endocarditis. In the entire series there were 4 patients with calcified valves. All of these fall into the present group of decompensation and cardiac death; one of them had recurrent vegetations and the other three had not. This, therefore, accounts for all but one of the 4 decompensated patients who did not have recurrent endocarditis.

Literature on Incidence of Recurrence in Pregnancy.

Two of the most important papers on this subject are those by Wagner[266] and Alders.[4] The largest group of authors consider that recurrent endocarditis is frequent in pregnancy, either as a result of excessive work of the heart or because of some other predisposition during pregnancy. Some of them speak of 'gestational endocarditis'. The estimates of frequency which are given range from 'very common' to 'an undue tendency in pregnancy'; Virchow,[253] Ollivier,[186] Berthiot,[14] Löhlein,[154] Dürr,[49] Virchow,[259, 260] MacDonald,[159] Müller[176] (cit. Alders), Schlayer,[221] Allyn,[6, 7] Phillips,[203] Handfield-Jones,[88] Meyer-Ruegg,[171] Tuszkai,[247] Polak,[207] Webster,[270] Kraus,[140] Freund,[66] Neuhof,[182] Eufinger,[54] Frey,[67] Schmidt,[223] Stumpel,[241] Kerr,[130] Jagic,[111, 112] Robinson,[215] Peham,[199] May.[166] A number of other references are given by Jensen (p. 214). Some of the more recent writers, however, take up the standpoint that there is not any predisposition to recurrent endocarditis during pregnancy: French and Hicks,[63] Fellner,[56] von Jaschke,[115, 116] Nelius,[180] Coombs,[36] Wagner,[266] Alders,[4] Parade.[194] There are even a few authors who maintain that it is of very rare occurrence in pregnancy: von Jaschke,[115, 116] Bauch,[9] Riehl.[214]

As Jensen points out (p. 214), the belief in a predisposition to recurrence as a result of pregnancy has so far lacked direct proof, and he himself is very sceptical on the subject. An attempt has, therefore, been made to ascertain from an analysis of the cases published in the literature whether the findings of

the present series can be considered typical of those in other parts of the world. There are certain general difficulties in such an analysis.

The terminology varies considerably in the literature; this is discussed by Jensen (pp. 207 to 211). Cases which appear to be actually recurrent endocarditis are reported sometimes as such, sometimes as ulcerative endocarditis, sometimes as subacute endocarditis, sometimes as acute endocarditis. For this reason the cases have, whenever possible, been analysed individually for the present study. Some of the earlier cases, when the authors employed terminology which is indefinite by modern standards, have been interpreted according to the classification in the present paper. Any errors in this re-diagnosis are probably insufficient to vitiate the main conclusion.

A further difficulty is that, in many of the records in the literature, the information given about the autopsy findings is very scanty and mention is not made of whether recurrent vegetations were present or not. In other records, this whole aspect has obviously been ignored as being without significance. These unsatisfactory cases cannot, however, be excluded from the statistical consideration.

The list below shows the findings recorded in the literature in 294 obstetric patients with chronic valve lesions which were examined post mortem. (The 510 fatal cases listed by Jensen, p. 120, include many without autopsy.) Cases with superimposed ulcerative lesions are excluded. As has been noted above, in many of the cases the autopsy notes are short, and mention is not made of whether recurrent vegetations were present or not. These patients are, however, all classed here as not having recurrence. Thus the incidence of 56 per cent shown in this list can only be accepted as a minimum figure; the true incidence was probably much nearer to the 79 per cent given in the present paper which is obtained from the specific investigation of detailed autopsy records.

Certain authors who report series of deaths in patients with chronic valvular disease note that recurrent endocarditis was present in some of their cases, but do not say how many of their deaths had been followed by autopsy. These 19 cases are obviously unsuitable for calculations of the incidence of recurrence, and are listed separately.

Smaller lists of this type have been given by Fromme,[73] Frey,[68] and Jensen. The data in Frey's table are based on autopsy material and are reasonably accurate. Jensen's table

(p. 213) contains certain misprints which to some extent invalidate the calculations. According to Jensen, Esch[53] criticised Fromme's data on the grounds that he included cases before 1902 when, he says, recurrent endocarditis was first described as a pathological entity. This criticism is not valid; the real fallacy in Fromme's figures is that he included a number of cases without autopsy among his total deaths. In fact, recurrent endocarditis was described as such by Virchow,[258] and there is little difference between the statistics of this century and the last. Thus, taking the data in the present list, recurrent endocarditis was recorded in 46 out of 89 obstetric autopsies up to 1899 and in 119 out of 205 autopsies since that date.

In the various papers from which these data are collected, there is a lack of control figures about recurrence in women not pregnant but of child-bearing age. Thus the statistics were left somewhat in the air, and Jensen (p. 213) quite reasonably does not accept that the figures he collected proved that the incidence of recurrence was increased in pregnancy. The data in the present series appear to supply this proof.

(*a*) *Patients with chronic valve lesions, excluding ulcerative endocarditis.*
(*b*) *Patients with recurrent endocarditis.*

	(*a*)	(*b*)		(*a*)	(*b*)
Alders[4]	18	12	Kautsky[125]	6	5
Bossler[19]	2	1	Kayser[126]	2	0
Breed and White[24] ...	2	1	Kiesin[131]	3	2
v. Broich[25]	5	2	Kreiss[141]	2	1
Bruhschwein[27]	5	3	Krummacker[142] ...	2	0
v. Coellen[34]	3	2	MacDonald[159]	4	1
Eisenbach[52]	3	1	Macé[164]	2	0
Eufinger[54]	8	6	Meyran[172]	16	9
Fellner[55]	6	5	Navratil[179]	2	1
French and Hicks[63] ...	3	0	Pagenstecher[193]	2	1
Freund[66]	10	5	Renaud[213]	13	7
Frey[68]	2	2	Schmidt[223]	4	4
Fritsch[72]	4	1	Schwarze[227]	2	1
Gerhardt[78]	4	4	Sommerbrodt[235] ...	2	0
Hagedorn[82]	5	2	Tunis[245]	4	3
Hart[93]	2	1	Virchow[258]	6	4
Hecker and Buhl[95] ...	2	1	Virchow[259]	5	5
Hensholdt[100]	4	4	Virchow[260]	4	4
Hochstetter[105]	2	0	Virchow[264]	3	1
Hochstetter[106]	2	2	Volkmann[265]	3	1
Hünermann[108]	2	2	Wagner[266]	8	6
v. Jaschke[114]	9	6	Walter[269]	8	6
Jensen[119]	4	3	v. Wenczel[272]	4	2
Katz[124]	8	2	Zinsstag[283]	3	1

Individual Chronic Cases.

With recurrence	Without recurrence
Ballantyne[8]	Allen and Bauer[5]
Bauch[9]	Bauch[10]
Berthiot[14]	Bazan[11]
Bottentuit[20]	Bennett[12]
Dressler and Fischer[46]	Binaut[15]
Duroziez[48]	Blau[17]
Freund[65]	Cameron[30]
Friedberg and Tartakower[70]	Duplant[47]
Füth[77]	Fisher[59]
Hart[92]	Fleischman[62]
v. Jaworski[118]	v. Guerard[80]
Jonen[123]	Jardine[113]
Kosminski[139]	Jess[121]
Litten[152]	Keller[127]
Mayor[167]	Lamb[144]
Nacke[177]	Lea[147]
Olshausen[187]	Leisse[149]
Paterson[198]	Leopold[151]
Prassulides[209]	Longaker[155]
Riehl[214]	Lvoff[156]
Rubinstein[218]	Lydston[157]
Schellong[220]	Meurer[169]
Schneider[224]	Müller[176]
Schwieger[228]	Ramsbotham[210]
Sée[229]	Reis and Frankenthal[212]
Violet and Peter[252]	Rosenberg[216]
Virchow[254]	Sommer[233]
Virchow[262]	Sommerbrodt[234]
Virchow[263]	Starling[238]
Wagner[267]	Stern[239]
Wedel[271]	Steven[240]
Wessner[274]	Trillat, Chavent and Colson[243]
	Vennemann[251]
	Wessinger[273]
	Wiesenthal[276]
	Wyatt[280]
	Zweifel[284]

Patients with recurrent endocarditis but without accurate or reliable data as to the total number of chronic cases with autopsy.

Daly and Strouse[41]	3	Rosenmund[217]	2
Fellner[56]	4	Schlayer[221]	1
Frigyesi[71]	3	Schlittler[222]	3
Petelen[201]	1	Ujma[248]	2

Valves Affected.

The valves affected by the recurrent vegetations are grouped in Table 23 according to the previous chronic valve lesion. For comparison the data from the control series of non-pregnant women are also given. The figures show the number of patients with each valve lesion.

Table 23.

Valve Incidence of Recurrent Endocarditis.

Obstetric patients

Recurrent lesion	Chronic lesion				
	M	AM	AMT	MT	A
Not present	7	5	0	0	2
M	24	6	0	0	0
AM	4	6	2	0	0
AMT	1	2	0	0	0
MT	3	0	0	2	0
A	1	0	0	0	0
Other	AMPT AMP	0	0	0	0

Non-pregnant women

Recurrent lesion	Chronic lesion				
	M	AM	AMT	MT	A
Not present	41	13	7	12	3
M	17	5	3	1	2
AM	6	13	2	0	0
AMT	1	3	1	0	0
MT	1	0	1	0	0
A	3	1	6	1	1
Other	AT AMP	AT	T AT	T T T TP AT	0

The incidence of recurrent endocarditis on each individual valve is shown in Table 24, grouped according to whether the recurrence was on a scarred valve or whether it was spreading to a previously undamaged valve. This latter condition is, of course, less common. It will be seen from these two tables that

the chief difference in valve incidence between women who are pregnant and those who are not, lies in the high incidence of recurrence on the previously scarred mitral valve in the pregnant women.

TABLE 24.

INCIDENCE OF RECURRENCE ON INDIVIDUAL VALVES.

	Obstetric patients with chronic valve lesions			Non-pregnant women with chronic valve lesions		
Previously scarred valve	Total cases	Recurrent lesions on this valve	Percentage	Total cases	Recurrent lesions on this valve	Percentage
Mitral	65	52	80	148	55	37
Aortic	23	10	43	64	29	45
Tricuspid ...	4	2	50	41	9	22
Previously undamaged valve						
Mitral	2	0	0	6	2	33
Aortic	44	8	18	90	14	16
Tricuspid ...	63	7	11	113	7	6

TIME OF ONSET.

The time at which the recurrent vegetations begin is of importance in any attempt to ascertain the aetiological factors. Table 33 shows that in half the cases the patient died before delivery or within one day afterwards: the recurrence in these cases must certainly have begun during pregnancy. In the great majority of the others, where death occurred in the puerperium, it appears probable that the recurrence began during pregnancy and continued through delivery and the early puerperium to the time of death. This view is based on the finding, in some of the cases, of early organization at the base of the vegetations, and also on the fact that the clinical condition of these patients during the pregnancy had been such that a recurrent endocarditis was a very strong probability at that time. The age of the occasional infarcts in systemic organs is not of assistance in this matter as the emboli presumably originated from thrombi in the auricular appendices. It is, of course, possible that recurrence may begin after delivery, but direct proof of this cannot

be given. The fact that most cases begin during pregnancy was noted by Virchow in 1872.

Evidence is not available to establish at what stage of pregnancy the recurrence usually develops. Any information about this matter is obscured by factors such as the type of death; a clue could be given by a sufficient number of patients who died of obstetric or other accidents at various stages of pregnancy, but those in the present series are only a small number and usually died at term. The data in Table 34 suggest that recurrence is possibly less frequent in the first half of pregnancy but the figures at that time are inadequate for any valid conclusions.

The influence of age is shown in Table 35; this has been discussed above. The influence of parity, shown in Table 36, is possibly related to the age factor.

Aetiology.

Recurrent endocarditis is presumably an indication of some active lesion in the valve, as evidenced by its tendency to spread to previously undamaged valves. But it does not appear to be part of an acute pancarditis, or at any rate of a pancarditis which can be recognized pathologically. The myocardium may show old scarring, particularly in the neighbourhood of the previously damaged valves, but active Aschoff nodes have not been found in any of the cases that were examined microscopically. Similarly, acute pericarditis is very rare (Jensen, p. 179); only one patient in the present series had any acute pericarditis, though 10 had old pericardial scars or adhesions which presumably dated from about the time of the original damage. Jensen (p. 160) makes some trenchant criticisms of the stock phrase that "it is the muscle that matters".

There were not any cases of acute rheumatism in the present series. The suggestion is sometimes raised that the agent of acute rheumatism may have been lying dormant in the heart since the last time the joints were inflamed and that this can be the cause of the recurrent endocarditis. It might be expected that the virulence of this agent would gradually become attenuated and that thus recurrent endocarditis would become less frequent as the time since the last attack of rheumatism became longer. The evidence on this matter is not conclusive as it is difficult to disentangle the significant factor of the age of the patient. In the present series 6 patients had had the last attack of acute rheumatism at 2 to 10 years before death; all of these

had recurrent endocarditis. Sixteen patients had had the last attack over 10 years before death; 14 of these had recurrent endocarditis. The differences cannot be considered significant.

Among the authors who suggest that the incidence of recurrent endocarditis in pregnancy is greater in young patients or those who have recently had rheumatism may be mentioned Simpson,[232] Virchow,[258] MacDonald,[159] Allyn,[6, 7] Handfield-Jones,[88] Polak,[207] Freund,[66] Fr. Jensen,[119] Alders,[4] and May.[166] Jensen (p. 214) regards it as probable but unproved that recent rheumatic infection is of unfavourable prognostic significance.

Various theories have been put forward to account for the great frequency of recurrence in pregnancy. A possible hormonal explanation is suggested by the fact that, as shown in the previous paper, recurrent endocarditis in decompensated patients is more common in women who are not pregnant than in men of corresponding ages. Biochemical or toxic disturbances have been held responsible, but without much evidence (Webster,[270] Eufinger,[54] Fr. Jensen[119]). A number of mechanical explanations have been given; the old theory of Virchow[258] and Dürr[49] of an abnormal narrowness of the aorta has been replaced by considerations of the increased cardiac output in pregnancy and of the changes in the circulation produced by the enlarging uterus. Apart from the general condition that the heart has to work harder in pregnancy, it is not clear how these factors would lead to recurrent endocarditis.

More plausible suggestions have been made that the condition is due to infections of various sorts. One of the common theories is that the recurrence is due to some form of puerperal sepsis (Osler,[191] Eisenbach,[52] von Jaschke,[115] Freund,[66] Cruickshank,[38] Tunis,[245] McIlroy and Rendle[160]). This view was strongly attacked by Virchow,[258, 259, 260] and subsequently by Kraus,[140] Frey,[68] and Alders.[4] The theory cannot be considered satisfactory in view of the fact, which is shown above, that the recurrence usually develops before delivery. In addition, as shown in Table 32, any association between recurrent endocarditis and puerperal sepsis can only be considered fortuitous.

Of recent years there has been a tendency to shift the blame to focal sepsis and other non-puerperal infections of teeth, tonsils, or kidneys, in order to explain the cases that obviously begin before delivery (Freund,[66] Cruickshank,[38] Fr. Jensen,[119] Jagic,[112] Alders,[4] von Jaschke,[117] Parade[194]). There is little reliable evidence with regard to teeth or tonsils; the facts given in Table 32 indicate that renal infections are not related to recurrence.

A toxic origin has also been suggested, based on the hypothesis that the toxaemias of pregnancy are due to a circulating toxin. An example of this reasoning is given by Willer[277] who reports a single case of acute (not recurrent) endocarditis associated with hypertensive toxaemia. The evidence given in Table 32 negatives the idea that these conditions are related.

Significance.

In the German literature there is almost universal agreement as to the seriousness of the condition. Eisenbach[52] and von Jaschke[117] maintain that it is invariably fatal. Many authors, while not taking so extreme a standpoint, consider that it is often fatal: Freund,[66] Benthin,[13] Eufinger,[54] Neuhof,[182] Frey,[69] Knauer,[135] Fr. Jensen,[119] Tunis,[245] Peham,[199] Heynemann,[103] and Parade.[194] Other authors class it as, at any rate, a very serious and important condition, and many of these are of the opinion that the seriousness is due to an associated myocarditis which leads to congestive failure: MacDonald,[159] Fromme,[73] Gerhardt,[78] Fellner,[56] Bauch,[9] Penshorn,[200] Frey,[68] Winter,[279] Knauer,[135] Jagic[111, 112] May,[166] Alders.[4] Very few critical voices are raised against these views. Wagner[266] agrees that the lesion is often found at autopsy in obstetric cardiac patients, but he is not prepared to accept this as any indication that it plays a part in causing death because, as he points out, the incidence in live obstetric patients with chronic valve lesions is unknown.

Many American authors (Jensen, p. 211) appear, on the other hand, to consider it a trivial ante-mortem development, "the so-called terminal verrucous endocarditis". This description carries unjustified implications. In the present series the vegetations were frequently found in patients who had died very rapidly of conditions which are usually not fatal, such as eclampsia or obstetric shock. It is thus not satisfactory to refer to them as terminal.

The fact that the vegetations may be found in patients whose hearts are not decompensated proves that, at any rate in their early stages, they do not necessarily cause congestive failure. But their almost invariable occurrence in decompensated patients points to some definite association. It is not clear whether the recurrent endocarditis causes or is caused by the decompensation, or whether both are the results of a third factor. As noted in the section on aetiology, there is not any satisfactory evidence that it is associated with a pancarditis. Thus the

immediate significance of the recurrent endocarditis is not yet elucidated.

Two points as to the possible secondary effects may be mentioned here; they are dealt with in more detail in the previous paper. Firstly, there is some evidence that the recurrent vegetations may act as the starting point for an ulcerative endocarditis. Secondly, if a patient recovers from recurrent endocarditis there is the possibility that it may lead to an increase of scarring in the previously damaged valves or, if it has spread to new valves, that it may lead to a fibrosis of these. This possibility has been discussed by Schlayer,[221] Tuszkai,[247] and Fr. Jensen.[119] But it is of interest that Jensen (pp. 184 to 196) could not find any convincing evidence that pregnancy shortens the expectation of life of patients with chronic valvular disease. Such a shortening might be expected if the recurrent endocarditis so commonly associated with pregnancy led to subsequent further scarring of valves.

Clinical Diagnosis.

Some authors report cases in which they have diagnosed recurrent endocarditis during life, but without giving details as to how they arrived at the diagnosis: Schlayer,[221] Tuszkai,[247] Fellner,[56] Freund,[65] Nelius.[180] Various clinical criteria have, however, been given by other authors; the points usually mentioned are: an insidious onset, tachycardia, subfebrile temperatures with a tendency to pyrexia on exertion, anaemia or leucocytosis, changes in the character of the cardiac murmurs, a tendency to congestive failure, a tendency to embolism, and a marked increase of the sedimentation rate. These symptoms are discussed by the following: Neuhof,[182] Frey,[67] Wagner,[266] Fr. Jensen,[119] Jagic,[111, 112] Peham,[199] Moritz,[175] May,[166] von Jaschke,[117] Parade.[194] The majority of these authors point out that the diagnosis is difficult and uncertain, but Fellner[56] considers that the symptoms are so severe that the condition can scarcely be overlooked.

The usual grounds on which the diagnosis is made are variations in pulse and temperature. It should, therefore, be pointed out that these criteria are not trustworthy, at any rate as they are ordinarily noted in hospital. The cases in the present series may be considered from this aspect in two categories, before and after delivery.

There were 23 patients who had been in hospital for a week or more before delivery, so that adequate records as to their

condition at that time are available. In 10 of these there were occasional slight rises of temperature to 99°F. or 100°F. about once a week. These were associated with, and possibly due to, mild respiratory or urinary infections in 7 cases; they were unaccounted for in the other 3 who were severely decompensated. All of these 10 had recurrent endocarditis. Occasional rises of temperature about once a week to 98.2°F. or 98.4°F. from an otherwise sustained level of about 97°F. occurred in 9 patients; 7 of them had recurrent endocarditis. The other 4 patients did not have variations of temperature of any kind; all 4 of them had recurrent lesions. The pulse-rate was rather lower in the 2 patients without recurrent lesions (averaging about 75 to 85) than in the patients with recurrence (averaging about 90 to 100). Auricular fibrillation occurred in 10 of the 21 patients with recurrent endocarditis and in both of the patients without this lesion.

There were 26 patients who were in hospital for 4 days or longer after delivery. Of the 6 patients who did not have any pyrexia after delivery, 5 had recurrence. The remaining 20 had various degrees of pyrexia; recurrent endocarditis was present in 16 of these, but in only 1 was there not any possible explanation of the pyrexia in uterine or other infection. In the 4 patients who did not have recurrent endocarditis there was some pyrexia in all, but it was explicable on some ground or other in 3. The pulse was rather rapid in most cases; this was usually related to the pyrexia.

A clinical diagnosis of recurrent endocarditis can thus not be based on variations of pulse or temperature, though, as shown earlier, it can reasonably be inferred from the age of the patient and the cardiac function. In this connexion it may be pointed out that Kinsey and White[132] find that, if careful observations are made, nearly every non-obstetric patient with congestive failure has some pyrexia. They ascribe this to the various complications, mainly in the lungs or heart.

SIMPLE ACUTE ENDOCARDITIS.

Simple acute endocarditis is used here to mean any vegetations which are not obviously ulcerative, and occurring in a heart in which there is not any macroscopically recognizable chronic valve lesion. As in recurrent endocarditis, the vegetations are small hyaline or fibrinoid masses about 1 to 4 mm. in

height. The difficulties in differentiating them from early ulcerative lesions have been discussed in the previous paper.

Table 25 shows that the incidence in these obstetric cases is practically the same as in the control series of women not pregnant, either taken in all or subdivided into age groups.

TABLE 25.

INCIDENCE OF SIMPLE ACUTE ENDOCARDITIS.

	Obstetric patients			Non-pregnant control series		
Age group	Total post-mortems	Cases of simple acute endocarditis	Percentage	Total post-mortems	Cases of simple acute endocarditis	Percentage
16 to 25	224	9	4.0	259	8	3.1
26 to 35	344	9	2.6	325	5	1.5
36 to 45	245	4	1.6	466	15	3.2
Total ...	813	22	2.7	1050	28	2.7

The aetiology is obscure. From Table 32 it will be seen that a relation cannot be established between the endocarditis and any of the common complications of pregnancy. One of the patients had chorea gravidarum. There were not any cases of active rheumatic fever, but 2 of the patients gave a history of having had rheumatism a few years before.

The time of onset of the endocarditis is also difficult to determine. As was shown in the previous paper, the age of the vegetations cannot be assessed accurately at autopsy, though there is some evidence that they can develop within a few days. Table 33 shows that nearly half the patients died during pregnancy or within a day after delivery; the lesions in these cases must certainly have begun before delivery. Nearly all the other patients died after the 5th day of the puerperium; the incidence at that time is not significantly greater than a chance one but some of these cases may have begun in the puerperium.

Tables 34, 35 and 36 show that there is not any significant relation to duration of pregnancy, age or parity.

Except in one case in which the patient developed cerebral embolism during anaesthesia, there is not any evidence that the acute endocarditis was a serious factor in causing death in the present series; all the remaining patients died from other diseases and the presence of the vegetations was only an incidental post-mortem finding. It is possible, however, that the vegetations were

associated with a valvulitis which might have led to subsequent scarring of the valves. If so, this would account for some of the cases of chronic valvular disease which appear clinically to date from a pregnancy.

The valves affected by simple acute endocarditis in pregnancy are compared with the corresponding data of the control group of women not pregnant, in Table 26. There is not any striking difference between the two sets of figures; single valve lesions affecting the aortic, and multiple valve lesions involving the pulmonary, are perhaps less common in the obstetric series.

TABLE 26.

VALVES AFFECTED BY SIMPLE ACUTE ENDOCARDITIS.

Age group	Valves affected by simple acute endocarditis				
	M	AM	AMT or MT	A	AMP or MP
Obstetric patients					
16 to 25	6	2	0	1	0
26 to 35	6	2	0	1	0
36 to 45	2	1	1	0	0
Control non-pregnant series					
16 to 25	5	1	0	0	2
26 to 35	0	1	1	3	0
36 to 45	10	1	1	2	1

It was not possible to make a diagnosis of the acute endocarditis during life. A number of the patients, who died in the puerperium, had pyrexia and tachycardia for several days before death, but there was always a sufficient explanation for this on non-cardiac grounds. Positive blood cultures were obtained in a few cases; these were ordinary puerperal septicaemias. It is, however, of interest to note that 3 of the patients who died in the puerperium had small infarcts in the spleen or kidneys and that 1 patient, previously mentioned, had a cerebral embolism during anaesthesia and died soon after delivery.

Literature.

As mentioned elsewhere, it is difficult to disentangle simple acute from ulcerative lesions in the discussions in the literature, and there is even much difficulty in differentiating primary simple acute from recurrent endocarditis. As a result the present review is confined merely to listing the probable cases of simple acute endocarditis recorded in the literature.

Ahlfeld[3]
Alders[4]—3 cases
Desnoyers[43]
Fitzgibbon[61]
Heiberg[97]
Heinrichsdorff[98]
Hocheisen[104]—2 cases
Hochstetter[105]
Hochstetter[106]
Hünermann[108]
Job[122]
Kayser[126]—2 cases
Keller[127]—2 cases
Keller[128]—2 cases
Klauer[134]
Kolisch[138]
May[166]
Meyer[170]
Milligan[174]
Navratil[179]
Neville[183]
Norton[185]—2 cases
Orth[189]
Rosenmund[217]
Schwarze[227]
Simpson[232]
Sommerbrodt[235]—2 cases
Tunis[245]
Velde and Volkmann[250]
Virchow[258]—7 cases
Virchow[259]
Virchow[260]—4 cases
Virchow[261]
Virchow[262]—2 cases
Virchow[263]
Virchow[264]—2 cases
Volkmann[265]
Willer[277]

ULCERATIVE ENDOCARDITIS.

The group of cases in which ulcerative endocarditis was found is subdivided according to the autopsy findings into 3 sections:

(*a*) Primary ulcerative endocarditis; i.e. without any recognizable evidence of a previous heart lesion; 4 cases.
(*b*) Ulcerative endocarditis superimposed on previously damaged valves; 6 cases.
(*c*) Subacute bacterial endocarditis, with or without a recognizable older valve lesion; 6 cases.

The criterion of ulcerative endocarditis which has been adopted is that the vegetations were massive and crumbling; in a few cases the valve segments were grossly ulcerated or perforated. In size, the vegetations were from 6 to 12 mm. or more in height; the cases examined histologically showed the typical structure and bacteriological content. It is possible that, in a few cases, lesions which have been classed in this paper as simple acute or recurrent may really have been the very early stages of ulcerative endocarditis; reference was made in the previous paper to the difficulty of differentiating these conditions. This is particularly the case in obstetric patients, in whom the non-ulcerative vegetations may be rather large and warty; it appears that these vegetations have been taken for ulcerative lesions by certain of the earlier pathologists, particularly in women who died of puerperal sepsis. On the other hand, there are certain cases with gross ulcerative lesions on

one valve while the other valves show small vegetations which have the naked-eye appearance of simple acute endocarditis. These small vegetations have presumably a similar aetiology to the grosser lesions, and are classed here as ulcerative.

The ordinary pathological criteria of subacute bacterial endocarditis have been adopted: vegetations of ulcerative type affecting the valves and spreading in addition over the surface of the left auricle.

Incidence.

Table 27 shows the incidence of ulcerative endocarditis in the present series, as compared with the incidence in the non-pregnant control series. As in the previous paper, ulcerative endocarditis superimposed on a previous chronic lesion is grouped with subacute bacterial endocarditis. It will be seen that the incidence of primary ulcerative endocarditis is higher in the control series of non-pregnant women than in the obstetric series; this is most obvious in the younger patients.

Table 27.

Incidence of Ulcerative Endocarditis.

Age group	Total post-mortems	Primary ulcerative	Percentage	Ulcerative on chronic, and subacute bacterial	Percentage
Obstetric cases					
16 to 25 ...	224	1	0.4	6	2.7
26 to 35 ...	344	2	0.6	3	0.9
36 to 45 ...	245	1	0.4	3	1.2
Total ...	813	4	0.5	12	1.5
Non-pregnant control series					
16 to 25 ...	259	11	4.2	6	2.3
26 to 35 ...	325	5	1.5	3	0.9
36 to 45 ...	466	2	0.4	6	1.3
Total ...	1050	18	1.7	15	1.4

The incidence of ulcerative on chronic endocarditis and subacute bacterial endocarditis is approximately the same in both groups when the actual numbers only are considered. There is,

however, a greater incidence in the obstetric group than in the women not pregnant relative to the total numbers of chronic valve lesions: 12 out of 82 pregnant women with chronic valve lesions (i.e. 14.6 per cent) as against 15 out of 169 non-pregnant women with chronic valve lesions (i.e. 8.9 per cent). This is probably due to the greater frequency of recurrent endocarditis in pregnancy; there is some statistical and histological evidence that recurrent vegetations often form the basis on which ulcerative vegetations are superimposed. Virchow[260] and Wilson[278] discuss this question.

There does not, however, appear to be any relation between simple acute endocarditis and primary ulcerative endocarditis; the former condition is as common in pregnant women as in those not pregnant, though the ulcerative lesion is relatively uncommon in pregnancy.

Time of Onset.

The cases are grouped in Table 28 to show the evidence as to whether the ulcerative lesion began before or after delivery. This is based on the time of death in relation to delivery, on the pathological findings, and on the clinical evidence studied in retrospect when the existence of ulcerative endocarditis and of the lesions

Table 28.

Time of Onset of Ulcerative Endocarditis.

Type of endocarditis	Onset before delivery				Possible onset after delivery
	Pathological proof	Clinical proof	Pathological probability	Clinical probability	
Primary ulcerative ...	0	2	0	1	1
Ulcerative on chronic	3	1	1	1	0
Subacute bacterial ...	3	1	1	1	0
Total	6	4	2	3	1

secondary to it had been shown at autopsy. The headings refer to the following groups:

(*a*) Patients with absolute pathological proof that the ulcerative endocarditis was present before delivery. These patients died either before delivery or within 12 hours afterwards.

(*b*) Patients with adequate clinical proof that the ulcerative endocarditis was present before delivery though death did not

occur until the puerperium. These patients had gross clinical evidence of cerebral or splenic embolism either before delivery or within two days afterwards; the infarcts were in all cases confirmed at autopsy. In addition there had been the usual clinical manifestations of ulcerative endocarditis during pregnancy.

(*c*) Patients with pathological evidence that the ulcerative endocarditis was probably present before delivery, though death did not occur until the puerperium. This evidence consists of valve lesions so gross that they could scarcely have developed in the short time between delivery and death, as judged from the time which appears to be required for the development of comparable lesions in non-obstetric patients. As examples, may be quoted cases of gross perforation of valve cusps found at autopsy 6 days after delivery or of very extensive vegetations of subacute bacterial endocarditis eleven days after delivery.

(*d*) Patients with clinical evidence that the ulcerative endocarditis which was found at death had probably been present before delivery, though death did not occur until the puerperium. This evidence consists of the development of cardiac murmurs before delivery in patients without previous heart lesions, or the occurrence of the typical evidence of septicaemia before delivery in cardiac patients without any other explanation being found, either clinically or at autopsy.

(*e*) Patients in whom there is not any satisfactory evidence of the time of onset of the ulcerative lesion, but with death so late in the puerperium (e.g. over 3 weeks) that the lesion could quite well have begun after delivery.

It will be seen from the table that in only one of the 16 cases can it reasonably be suggested that the ulcerative lesion began after delivery.

Association with Other Diseases or with Obstetric Factors.

Throughout most of the literature ulcerative endocarditis has been ascribed as secondary to some septic focus. Whenever the patient happened also to have puerperal sepsis at death, this condition has usually been blamed as the primary source, irrespective of the fact, which has just been shown, that the ulcerative endocarditis begins in nearly every case before delivery. It is, therefore, important to note that the evidence in Table 32 does not show anything more than a purely chance association of any form of ulcerative endocarditis with puerperal sepsis, pyelonephritis,

or hypertensive toxaemia. These conditions, therefore, cannot be regarded as causes, or even effects, of ulcerative endocarditis.

Among the patients with ulcerative on chronic, or subacute bacterial endocarditis, 7 had a previous history of rheumatism, 4 denied any such history, and in the remaining case information is lacking. These figures are not significantly different from those in patients with chronic valve lesions not complicated by ulcerative endocarditis.

The only point of importance among the obstetric factors shown in Tables 33, 34, 35 and 36, is the duration of the pregnancy; patients with ulcerative endocarditis superimposed on an old lesion or with subacute bacterial endocarditis show a significant tendency to abortion or premature delivery. Mengert[168] is not of this opinion. There is not any significant relation of the various forms of ulcerative endocarditis to age, parity, or to the time of delivery.

Valves Affected.

Table 29 shows the valves affected by ulcerative endocarditis in the obstetric series as compared with the control series of women

Table 29.

Valves Affected by Ulcerative Endocarditis.

Ulcerative valve lesion	Obstetric series Chronic valve lesions				
	None	M	AM	AMT or MT	A or others
None	724	44	19	5	2
M	1	5	0	0	0
AM	2	1	4	0	0
AMT or MT ...	1	1	0	0	0
Others	0	0	1	0	0

Ulcerative valve lesion	Non-pregnant control series Chronic valve lesion				
	None	M	AM	AMT or MT	A or others
None	861	71	36	41	6
M	10	5	0	1	0
AM	5	1	1	0	2
AMT or MT ...	2	2	0	0	0
Others	1	1	1	0	1

not pregnant. As mentioned above, subacute bacterial lesions are classified as occurring on chronically damaged valves. The valves noted as affected by ulcerative lesions include not only the gross vegetations but also the lesser vegetations which are sometimes found on the other valves.

It will be seen that there is not any significant difference between the valve incidence in the pregnant or non-pregnant women, as regards either the ulcerative lesions or the previous chronic lesions on which they are superimposed.

Table 30 shows that there is a similar proportionate incidence of ulcerative lesions on the various individual scarred valves in pregnant and in non-pregnant women, though, of course, the actual figures are relatively higher in the former.

TABLE 30.

INCIDENCE OF ULCERATIVE ENDOCARDITIS ON CHRONIC VALVE LESIONS.

	Obstetric patients			Non-pregnant control series		
	Total chronic lesions	Total with ulcerative lesions	Percentage	Total chronic lesions	Total with ulcerative lesions	Percentage
Mitral	80	11	13.8	160	10	6.3
Aortic	28	4	14.3	89	4	4.5
Tricuspid ...	5	0	0	42	0	0

SYMPTOMS AND MANNER OF DEATH.

Primary Ulcerative Endocarditis.

The condition of the 3 patients whose ulcerative endocarditis probably began before delivery was not constant during pregnancy; one patient had dyspnoea, one had cardiac collapses and evidences of emboli; the other was apparently well. Their pulse-rates ranged from 100 to 120, but the temperatures were normal. They all developed pyrexia immediately after delivery. Two of them died of cerebral embolism and the third of pulmonary infarcts with gross pleural effusion. In the fourth patient, who may have developed the ulcerative lesion in the puerperium, the pyrexia began only 7 days after delivery; she died with pyaemia and multiple infarcts. It is perhaps of interest that 3 of these patients had purulent vaginal discharge during the pregnancy.

Ulcerative on Chronic Endocarditis.

The most constant occurrence was a particularly severe type of congestive failure which began usually at about 18 weeks, though in one case it developed during the first few weeks of pregnancy. This progressed rapidly and caused death after about a further 8 weeks. It was usually associated with evidences of septicaemia, and a temperature before delivery either swinging from 99°F. to 102°F. or, more commonly, ranging from 97°F. to 99°F. with an occasional rise, about once a week, to 102°F. or 103°F. After delivery the temperature rose in all cases, and swung between 99°F. and 103°F. In one case there was neither pyrexia nor congestive failure before delivery; the patient died of cerebral embolism.

Subacute Bacterial Endocarditis.

The usual clinical course of these cases was as follows: During the first half of the pregnancy the patient gradually developed some anorexia, loss of weight, and cough with some sputum. At about 18 to 24 weeks she became dyspnoeic; this progressed rapidly and became very severe; it was sometimes accompanied by oedema of the labia or legs. There was usually a low grade pyrexia, the temperature swinging from 97°F. to 98.6°F. or 99°F., with an occasional rise to 100°F. or 101°F. about once a week. The pulse was often rapid; 100, 120, or faster. In one of the patients pyrexia did not occur at any time, and the pulse-rate was only 80 to 90 per minute. The cases with examination of the blood showed a streptococcus viridans septicaemia and a secondary anaemia without much leucocytosis. Three of these patients died of cerebral embolism. The others died of progressive decompensation or acute heart failure; they had multiple infarcts of the spleen and kidneys but not of the brain.

Literature on Ulcerative Endocarditis.

Jensen (p. 284) lists a series of accepted cases of bacterial endocarditis related to pregnancy. A few of the cases in his list are rather uncertain and may actually have been simple recurrent endocarditis; these are not included in the following list. A certain number of other cases with autopsy not mentioned by Jensen are, however, included here. It is to be emphasized that the distinction of simple from ulcerative vegetations in cases published in the literature is not very easy and that a number of errors may be present in this list. The nomenclature varies from author to

author; Jensen does not discriminate between subacute bacterial endocarditis and ulcerative endocarditis. As far as possible the cases in the literature have been interpreted here according to the descriptions given in this paper.

Primary ulcerative endocarditis

Bossler[19]
Bruhschwein[27] (ref. Jensen)
Bumke[28]
Dabney and Harris[39]
Eichhorst[51]
Fruhinsholz and Michon[74]
Fry[76]
Guyot[81]
Harrar[90]
Heiberg[96]
Hocheisen[104]
Hochstetter[105]
Hummerich[107]—2 cases
Hünermann[108]
Ingram and Longridge[110]
Kayser[126]
Klauer[133]
Klauer[134]
Kolb[137]
Lancereaux[146]—7 cases
Lebert[148]—2 cases
Litten[152]
Meyer[170]
Milian[173]
Olshausen[187]
Orth[189]
Pfahl[202]—2 cases
Pichon and Turnesco[206]
Ruiz and Garcia[219]—4 cases
Sigwart[231]—7 cases
Sommer[233]
Tuckwell[244]
Virchow[254]
Virchow[256]
Virchow[257]—4 cases
Virchow[258]
Virchow[259]
Virchow[260]
Virchow[261]—6 cases
Virchow[262]
Virchow[263]—2 cases
Virchow[264]—2 cases
Young, R. A.[282]

Ulcerative endocarditis superimposed on chronic

Alders[4]—2 cases
Caussade and le Rasle[33]
Croom[37]
Fitzgerald[60]
French and Hicks[63]
Fruhinsholz, Michon and Lévy[75]
Kelynack[129]—3 cases
Kobacker[136]
Litten[152]—3 cases
Orth[190]
Phillips[204]
Pic and Gruber[205]
Porak[208]—2 cases
Schlittler[222]
Simpson[232]—4 cases
Virchow[259]—4 cases
Virchow[260]
Virchow[262]
Virchow[263]
Westphal[275]

Subacute bacterial endocarditis

Bradford[21]
Felsen, Schumer and Osofsky[57]
Fry[76]
Job[122]—2 cases
MacRae[163]—2 cases
Mengert[168]
Page and Campbell[192]
Virchow[260]
Walser[268]

Table 31 shows the cases in this series subdivided according to the date of publication, before or after 1900. The total numbers of published cases of chronic valvular disease in each period are given as a standard of comparison; they are obtained from the lists in the sections on recurrent and ulcerative endocarditis.

TABLE 31.

INCIDENCE OF ULCERATIVE ENDOCARDITIS RECORDED IN OLD AND RECENT LITERATURE.

Endocarditis	Literature to 1899	Literature since 1900	Present data
All chronic lesions, including ulcerative	111	245	82
All ulcerative lesions ...	70	45	16
Chronic with ulcerative ...	20	12	6
Subacute bacterial	1	10	6
Primary ulcerative	49	23	4

Measured against this yardstick, it will be seen that the reported incidence of all kinds of ulcerative endocarditis was more than three times as great before 1900 as since then. When these ulcerative lesions are subdivided into the three types, it is seen that the main difference is in the enormous incidence of primary ulcerative lesions before 1900. The usual histories of these older cases were of a very late onset of puerperal pyrexia and death 6 to 8 weeks after delivery (see Osler[191]). It is possible that these cases were a definite clinical entity peculiar to the pre-antiseptic days of obstetrics and comparable with such conditions as hospital gangrene or wound erysipelas. Cases of this kind were not found in the present series and it may be questioned whether they occur at all under modern conditions. This may account partly for the reduction of the death-rate in cardiac patients in recent years which is noted by Jensen (p. 127).

Literature on Aetiology.

Jensen (pp. 279 to 290) gives a good review of the development of knowledge of ulcerative endocarditis in relation to obstetrics, and only a few points need to be mentioned.

The association of ulcerative endocarditis with puerperal sepsis has been remarked on by numerous authors (Virchow,[258] Olshausen,[187] Freund,[64] Meyer-Ruegg,[171] Croom,[37] Vaquez,[249] Wagner,[266] Sigwart,[231] Cruickshank,[38] Schottmüller,[225] Dietrich,[44]

Donath and Saxl,[45] Alders[4]). It has been considered that this is particularly the case after abortions (Osler,[191] Ruiz and Garcia,[219] McIlroy and Rendle[160]). Sepsis of non-puerperal type, such as oral, renal or intestinal, has been blamed by Cameron,[29] Caussade and le Rasle,[33] and Cruickshank.[38] Many of these views appear to be based on the conditions obtaining in the last century.

The fact that the disease may develop before delivery has, however, been recognized by various authors (MacDonald,[159] Guyot,[81] Gerhardt[78]) and Jensen (pp. 283 to 285) gives a table showing that nearly all cases occur before delivery.

The rarity of subacute bacterial endocarditis in pregnancy is noted by many authors, including Walser,[268] Mengert,[168] Terwilliger,[242] and MacRae.[163]

POTENTIALLY RELATED FACTORS.

Association of Valve Lesions with Other Diseases.

When certain other pathological conditions are found in patients who have valve lesions at death, it is often suggested that the heart lesion may have caused or been caused by the intercurrent disease. This applies particularly to acute valve lesions. The most satisfactory way of investigating this point is to ascertain, in a large group of patients, the percentage who have the intercurrent disease and the percentage who have any particular variety of valve lesion. It is then a simple matter to calculate the number who should have both the intercurrent disease and the valve lesion together, if this association were purely due to chance. A comparison of this number with the number who actually have both conditions together gives an indication whether the actual association is fortuitous or not.

It is admittedly possible that minor grades of certain diseases (e.g. pyelitis) may not be recognized clinically or at autopsy, but this source of error applies equally to the gross incidence of the disease and to its association with valve lesions. The basis of the comparisons is thus unaffected.

Pyelonephritis or pyelitis was found at autopsy in 79 of the 813 patients. Thus, among the 105 patients with valve lesions of various kinds, 10.2 would have, by pure chance, an association of pyelonephritis and valvular disease. The actual number with such an association was 8.

Eclamptic fits had occurred in 83 of the 813 patients; the chance association with valve lesions is thus 10.7. The actual association was 6.

Hypertensive toxaemia, varying from quite mild cases up to severe pre-eclampsia (but not including eclampsia), was present in 70 of the last 200 patients examined post mortem. This analysis is restricted to recent cases because the clinical histories of some of the earlier cases are not sufficiently detailed about the matter. In the 200 cases there were 32 patients with valvular lesions, so that there should be a chance association with hypertensive toxaemia in 11.2 cases. The actual association was 11.

Puerperal sepsis is considered only in the group of 345 patients who died later than 24 hours after delivery and who were thus liable to have recognizable sepsis. The cases classified as septic ranged from those with slight foetor of the placental clot up to gross purulent endometritis, thrombophlebitis, parametrial infection, or peritonitis. The number of these septic cases was 200; the number of patients with any valve lesion was 56. The chance association would thus be 32.4 cases; the actual association was 26.

In Table 32 these various factors are considered in relation to the types of valvular disease. The actual numbers of cases with each combination are shown, and in parallel columns are given the numbers that would occur by a pure chance association. (The groups are not the same, so that the proportions with each valve lesion vary from group to group.)

TABLE 32.

INCIDENCE OF VARIOUS KINDS OF ENDOCARDITIS IN ASSOCIATION WITH OTHER DISEASES.

Type of endocarditis	Pyelonephritis		Eclampsia		Hypertensive toxaemia		Puerperal sepsis	
	Actual	Chance	Actual	Chance	Actual	Chance	Actual	Chance
Chronic with recurrent	2	5.1	4	5.4	6	6.6	12	15.6
Chronic without recurrent	0	1.4	0	1.4	1	1.1	3	4.6
Simple acute	3	2.1	1	2.3	4	2.5	6	6.4
Primary ulcerative	2	0.4	0	0.4	0	0.6	2	2.3
Ulcerative on chronic, and subacute bacterial	1	1.2	1	1.2	0	0.4	3	3.5

While the findings of the present study do not have any high mathematical significance, their general import is clear. There are not any significant differences between the actual and the chance associations shown in the table, though there is some suggestion that chronic valve lesions are less frequently associated with pyelonephritis or puerperal sepsis than would be expected by pure chance. This is probably due to the fact that dystocia, which is a common cause of acute cysto-pyelitis and of puerperal sepsis in other patients, is usually avoided in cardiac patients. As noted in earlier sections, it is thus clear that the various factors which have been considered do not have anything to do with any form of valvular disease. A comparable analysis of the effect of infections of the throat or teeth is needed in view of the opinions expressed by various authors mentioned earlier, but data are not available in the present series.

Jensen discusses most of these points. He concludes (pp. 147 and 238) that evidence is lacking that valvular disease of the heart is associated with an increase in the death-rate from puerperal sepsis. This is in agreement with the views of Bjerring,[16] but against those of Freund[66] and Wagner.[266] He does not discuss in detail any relation of ulcerative endocarditis to sepsis. He does not find any relation between valvular disease and hypertensive toxaemia or eclampsia (pp. 147 and 216). He considers, however, that pneumonia and pulmonary infarcts are particularly common in valvular disease (pp. 147 and 233). This is in agreement with the present findings; in addition to the patients noted specifically as having died of cardiac pulmonary complications, there were many who had pulmonary infarcts which were a contributory cause of death.

Jensen (p. 235) also raises the question of the association of tuberculosis with heart disease in pregnancy. The present data are insufficient to provide definite conclusions, but they do not give any suggestion that pulmonary tuberculosis has a specific relation to cardiac disease. Among the 705 control obstetric patients without valve lesions 10 had pulmonary tuberculosis; among the 108 patients with valve lesions 2 had pulmonary tuberculosis. The valve lesions were in one case a slight mitral stenosis with death from sepsis but without any decompensation, and in the other case a simple acute endocarditis affecting the mitral and aortic valves.

Relation of Valve Lesions to Obstetric Factors.

The other factors, such as the age or parity of the patient, the duration of the pregnancy, and the time of death in relation to delivery, are shown in Tables 33, 34, 35 and 36, in relation to the type of endocarditis. These tables do not include the 3 chronic cases in which information about recurrence was not available. The main conclusions from these tables have been shown earlier in the relevant sections.

Table 33.

Relation of Death to Delivery with Various Kinds of Endocarditis.

Type of endocarditis	Time of death					
	During pregnancy	During labour	Days after delivery			
			To 1	2 to 4	5 to 10	Over 10
Control obstetric patients without any valve lesions	71	56	296	70	143	69
Chronic with recurrent	11	4	12	5	9	12
Chronic without recurrent	1	1	6	2	3	1
Simple acute	2	2	6	1	6	5
Primary ulcerative	0	0	0	1	1	2
Ulcerative on chronic, or subacute bacterial	3	2	1	2	1	3

Table 34.

Duration of Pregnancy at Death or Delivery in Various Kinds of Endocarditis.

Type of endocarditis	Duration of pregnancy in weeks			
	To 19	20 to 29	30 to 35	36 and over
Control obstetric patients without any valve lesions	56	42	106	501
Chronic with recurrent	1	4	18	30
Chronic without recurrent	2	0	3	9
Simple acute	3	1	5	13
Primary ulcerative	0	1	1	2
Ulcerative on chronic, or subacute bacterial	3	4	4	1

TABLE 35.

AGE AT DEATH IN VARIOUS KINDS OF ENDOCARDITIS.

Type of endocarditis	Age		
	16 to 25	26 to 35	36 to 45
Control obstetric patients without any valve lesions	190	303	212
Chronic with recurrent	12	28	13
Chronic without recurrent	0	6	8
Simple acute	9	9	4
Primary ulcerative	1	2	1
Ulcerative on chronic, or subacute bacterial	6	3	3

TABLE 36.

PARITY AT DEATH IN VARIOUS KINDS OF ENDOCARDITIS.

Type of endocarditis	Number of pregnancies		
	1	2 and 3	4 and over
Control obstetric patients without any valve lesions	282	169	254
Chronic with recurrent	25	13	15
Chronic without recurrent	3	2	9
Simple acute	9	9	4
Primary ulcerative	1	0	3
Ulcerative on chronic, or subacute bacterial	6	4	2

OTHER CARDIAC CONDITIONS.

Hypertensive Cardiac Failure.

Decompensation of the hypertrophied heart of chronic hypertension is of importance, as it may be mistaken for chronic valvular disease, but a full consideration of this subject is outside the scope of the present paper (see Jensen, pp. 314 to 332). Brief reference may, however, be made to 6 rather outstanding examples in the present series. The patients were all old multiparae; they had various degrees of congestive failure for several weeks, combined with severe hypertension and evidences of renal insufficiency; murmurs suggesting mitral lesions were found in 5 cases. Three of them died of progressive decompensation, one of a septic pulmonary infarct, and two of rupture of the arch of the aorta

(see Jensen, p. 329). In all cases the heart was very large, 430 to 530 gms., and the left ventricle showed gross hypertrophy, but organic valve lesions were not found.

Cardiac Neurosis.

In Group III of his Heart Classification, Hamilton[86] includes patients with cardiac symptoms, but without any organic cardiac or vascular disease. These patients very rarely die. It is, therefore, of interest to record one such case in the present series. The patient, a 4 para aged 30, complained of dyspnoea and a choking sensation ever since the beginning of pregnancy. The pulse, temperature, and blood-pressure were normal, but a systolic murmur was present at the apex. The symptoms became worse, so abdominal hysterotomy was performed at 24 weeks; the patient died of intraperitoneal haemorrhage 2 hours later. At autopsy the heart was normal in every way.

Atheroma and Syphilis.

As would be expected from the age of the patients, senile changes of the aortic valves, of the kind usually classed as atheromatous, were not found. The small lipoid plaques sometimes seen on the anterior cusp of the mitral valve are not taken into consideration here.

Syphilitic lesions were also very rare. Only one definite case was found in the present series: a multipara aged 41. This is in striking contrast to the conditions in certain foreign clinics (Jensen, p. 291).

Congenital Heart Disease.

There were not any cases of congenital heart disease in the present series. This is not surprising. Jensen (p. 296) found 2 deaths from congenital heart disease in 3,378 clinical cases of chronic heart disease in pregnancy. The present paper is based on a calculated series of 3,440 cases of chronic heart disease but less than half the patients who died were examined post mortem. Thus not more than one case of congenital heart disease would be expected in the present series of autopsies.

SUMMARY.

An analysis was made of the clinical and pathological findings in 108 obstetric patients who showed acute or chronic lesions of the heart valves at autopsy. For purposes of control these were

compared with the autopsy findings in 215 women of child-bearing age who were not pregnant and who had similar valve lesions, and in 705 obstetric patients with normal valves. The following conclusions were drawn:

Chronic rheumatic valvular disease is present in 1.5 per cent of all obstetric patients in this locality. The mitral and aortic valves are involved with about the same frequency as in women not pregnant, but tricuspid lesions are found at autopsy much less commonly than in women not pregnant. The clinical diagnosis of particular chronic valve lesions is much better when heart symptoms are present than when they are not present, but a correct diagnosis is made in less than half of the cases. The difficulties in clinical diagnosis make it impossible to place full reliance on studies based on clinical data alone.

The mortality in women with chronic valve lesions was 6.3 per cent; 0.9 being due to superimposed ulcerative endocarditis, 2.9 per cent to other cardiac causes, and 2.5 per cent to non-cardiac complications.

Nearly half the patients had had some evidence of congestive failure which usually began either in the first few weeks of pregnancy or at about 6 months. This was related to the type of valve lesion, severe mitral stenosis and mitral stenosis combined with aortic stenosis being the most serious, while incompetence of valves was of less significance. The degree of hypertrophy of the heart did not appear to be a factor of importance in causing decompensation.

Deaths during or immediately after labour are usually not due to the progressive exhaustion of a badly decompensated heart, but are in most cases catastrophic acute heart failures in patients who have been either not or only slightly decompensated. Such acute heart failures are not satisfactorily described as acute pulmonary oedema, because the lungs are oedematous at autopsy in nearly all patients suffering from heart disease, whatever the manner of death.

The deaths during pregnancy or the late puerperium are several times as common as in patients not pregnant.

While many patients have never had congestive failure before, any patient whose heart becomes decompensated in a pregnancy will almost inevitably have the same condition in every subsequent pregnancy.

The American Heart Association Classification is of some value when it is based on the patient's condition in the last quarter

of pregnancy, but it is not of help in assessing the prognosis before this stage of pregnancy.

The common belief that decompensation of the heart is related to a myocarditis or acute pancarditis does not rest on a satisfactory basis. On the other hand, simple recurrent endocarditis superimposed on old chronic valve lesions shows a very much higher incidence in pregnant women than in those not pregnant, and in those whose heart is decompensated than in those in whom it is not. The reason for the very high incidence in obstetric cases is not clear, but the recurrence appears to develop in the course of pregnancy and not in the puerperium. Recurrent endocarditis cannot be diagnosed satisfactorily during life except by inference. Though its exact significance remains to be established, it is an important complication of chronic valve lesions.

Simple acute endocarditis occurs in pregnancy with about the same frequency as in women not pregnant, and does not present any special features.

Ulcerative endocarditis superimposed on old chronic valve lesions and subacute bacterial endocarditis are rather commoner in pregnant women than in those not pregnant. These conditions develop during the course of pregnancy and not in the puerperium. They may be based on recurrent endocarditis. They lead to a particularly severe type of decompensation.

Primary ulcerative endocarditis (without previous chronic valve lesion) is very much less common in pregnant women than in women not pregnant. It appears from the literature that an ulcerative endocarditis developing in the puerperium was very common in the pre-antiseptic days of obstetrics, but this type of valve lesion does not seem to occur nowadays.

A patient who has any kind of valve lesion, chronic, recurrent, acute, or ulcerative, may also have pyelonephritis, hypertensive toxaemia, eclampsia, or puerperal sepsis, but these diseases do not have any relation to the valve lesion, either as cause or effect.

Deaths associated with congenital heart disease, cardiac neurosis, or syphilis or primary sclerosis of the aortic valve are rare.

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A Granulosa-cell Tumour of the Ovary with remarkable Hyperplasia of the Uterus.

BY

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THE following case illustrates the classical features of the granulosa-cell tumour of the ovary which had probably been present for about 4 years, so that its endocrine action was pronounced.

In addition, other pathological conditions—namely, tuberculosis of the Fallopian tube and a parovarian cyst—were present. The specimen is now in the museum of University College Hospital Medical School. (Fig. 1.)

Clinical history. Age 67; nullipara. The patient had been an inmate of Leavesden Mental Hospital for the last 6 years suffering from mild delusional insanity. She had delusions that she was "Lady S——" and was "visited at night by a spiritual husband, Dr. S——" and, latterly, that she was going to have triplets. In April, 1935, she was noted as having "menstruated on 36 days during the last 4 months." On examination the uterus was not enlarged, but no other abnormality in the pelvis was found. In June, 1935, the patient started to have a blood-stained discharge, and the uterus was found to be slightly enlarged. In November, 1935, profuse uterine bleeding occurred, and this continued at intervals during the following year. In June, 1937, oedema of the left leg appeared, and the bleeding was now almost continuous and often severe.

Irregular bleeding continued till September, 1939, and a firm mass was then felt rising from the pelvis somewhat to the right of the midline. On pelvic examination an enlarged uterus was felt drawn upwards by a solid tumour lying to the right of it. The cervical canal was dilated, and through it projected a large polypus. Blood was seen issuing from the uterus.

A tentative diagnosis of granulosa-cell tumour was made. As the case occurred in the early days of the war, blood and urinary oestrone estimations were difficult to arrange and were dispensed with.

At the operation the uterus was found to be enlarged to about the size of a 12 weeks' to a 14 weeks' gestation, and a lobulated ovarian tumour, somewhat adherent, was present on the right side. There was a small nodule of what appeared to be growth in the right Fallopian tube and a parovarian cyst, the size of a hen's egg, on the left side. Ascites or other signs of metastasis were absent. Total hysterectomy and bilateral salpingo-oöphorectomy were performed.

Convalescence was uneventful. The mammae did not secrete after operation. The delusions remained unaltered except that the patient no longer thought she was going to have triplets.

Description of Specimen.

The uterus is enlarged to the size of a 12 to 14 weeks' gestation. The enlargement is due partly to hyperplasia of the myometrium, the walls of the uterus being about $2\frac{1}{2}$ inches thick, and partly to enormous hyperplasia of the endometrium which forms a trabeculated and mammillated mass sprouting through the cervix. The general appearance resembles that of an advanced carcinoma of the body of the uterus. (Fig. 1.)

The ovarian tumour, which is rubbery in consistence, measures approximately $8\frac{1}{2}$ by $5\frac{1}{2}$ by 4 inches. The surface is pale lobulated with few adhesions.

On section, the tumour is chiefly solid with numerous cystic areas. The cut surface is pale with areas of necrosis. One of the cystic spaces has a well-formed fibrous wall.

A small nodule in the Fallopian tube of the same (right) side imparted a gritty sensation when cut with a knife. It has proved to be a tuberculous lesion and not secondary growth as was thought at operation. A parovarian cyst about $2\frac{1}{2}$ inches in diameter is present on the opposite (left) side.

Microscopic Appearance.

The endometrium shows diffuse polypoid hyperplasia. The glands show great epithelial proliferation and their mouths are in some cases dilated. (Fig. 2.) Some are cystic. A degree of metaplasia is present in some areas of a type resembling a carcinoma. The stroma is increased. (Fig. 2.)

The nodule in the tube is a typical tuberculous lesion with giant cells.

A large part of the ovarian tumour consists of a diffuse growth of the so-called sarcomatous type of granulosa-cell tumour

FIGURE I.

FIGURE II. (×25).

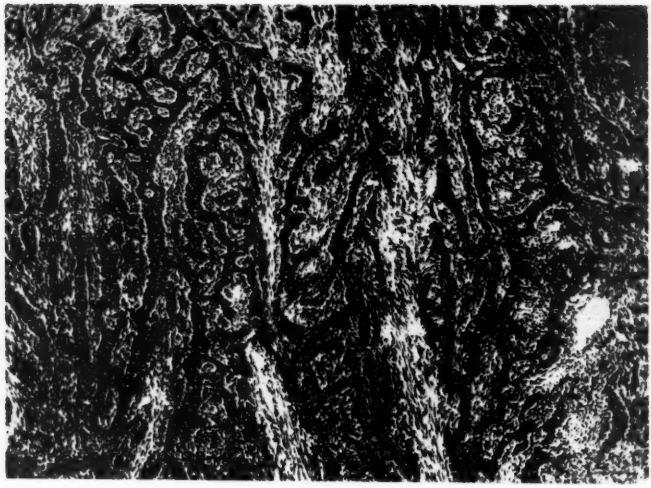

FIGURE III.

FIGURE IV.

which shows in many places such a degree of metaplasia that its recognition is difficult. This portion of the tumour seems to have been most secretory, for large pools of secretion, staining pink with eosin, are visible among the cells. Blood-vessels are very numerous, and the tumour cells seem to radiate out from their walls.

Trabecular, cylindroid and folliculoid forms were present in smaller areas of the tumour. The trabecular show the well-known wavy or moiré pattern (Fig. 3). The folliculoid type (Fig. 4) was found only in small areas. The characteristic islets of secretion (dissolved out in these sections) can be seen lying eccentrically in the granulosa cells. Call-Exner bodies are well formed in the latter types but infrequent in the diffuse portions.

Comments on the Case.

Besides being a collection of various pathological conditions the case is of interest in the following respects:

1. The striking response of both myometrium and endometrium to the hormone secreted by the tumour, partly due to its long standing. The changes in the endometrium are very different from the simple gruyère cheese pattern of metropathia. The fact that the epithelial proliferation and metaplasia resemble in some places a carcinoma is of interest when considered in connexion with the possible association of excessive or abnormal oestrin secretion and carcinoma formation.

2. A presumably large secretion of blood oestrone was suddenly terminated by operation. A similar mechanism occurring after delivery (by removal of placental oestrone?) and is said to be the stimulus to prolactin secretion by the pituitary after previous sensitization of the breasts by the rising blood oestrone. Yet in this case mammary activity was absent before and after operation. The patient's age, 67, however, may account for this.

3. Though the tumour had attained the size of a foetal head at term, signs of metastasis were absent. This confirms the view generally held that these tumours are of low malignancy.

4. In studying several of these tumours the writer has been impressed by the necessity of making numerous sections from different portions of every specimen, since otherwise only a portion showing a diffuse or atypical growth lacking Call-Exner bodies may be examined, making the tumour difficult to recog-

nize. The more striking forms such as the folliculoid one may be present only in small areas.

5. The association of erotic delusions is probably fortuitous.

I have to thank Dr. R. M. Stewart, Medical Superintendent of Leavesden Mental Hospital, for permission to publish the case. Dr. Vines kindly examined the sections, and further sections and microphotographs were prepared for me by Mr. F. R. Hill of the Leavesden Hospital pathological laboratory.

Unilateral Twin Tubal Pregnancy with coincident Intra-uterine Pregnancy

BY

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COMBINED intra-uterine and tubal pregnancy has not been reported frequently, and is regarded as a somewhat unusual obstetrical entity. The frequency and peculiarities of the condition are fully dealt with later.

Bilateral tubal twin pregnancy, either simultaneous or compound, has also been recorded. Unilateral twin tubal pregnancy is not nearly so common, and seems to be very unusual when found in association with coincident intra-uterine pregnancy.

As far as is known the pregnancies in the case about to be recorded were simultaneous:

A primigravida, aged 34 years and already married for 18 months, menstruated for the last time on the 25th of October, 1939. From the onset there was morning sickness, but in particular a history of some fresh, red vaginal bleeding on December 10th. This was painless, being followed by brownish vaginal discharge, which persisted, and was still present when she was examined on the 5th of January, 1940.

The uterus was found to be enlarged to about 6 or 8 weeks' size but not typically soft, nor was the blueing of the vulva or Hegar's sign well marked. The position of the uterus was normal, but a note was made to the effect that there might be a small interstitial fibroid in the right cornu and that there was an indefinite, slightly fixed cystic fullness behind the right broad ligament. The diagnosis appeared to rest between a missed abortion with some intra-pelvic abnormality or a tubal mole. A history suggestive of appendicitis or abdominal discomfort could not be obtained.

On January 10th there was a spontaneous and complete uterine abortion without undue bleeding or pain, and the ovum corresponded to about 2 months' development. Recovery was normal, without curettage or other interference, but on January 26th a small, fresh, painless vaginal bleeding occurred and lasted for about 2 hours.

On February 2nd vaginal examination revealed the uterus still in normal position, slightly softened, with a doubtful Hegar's sign. The right-sided pelvic tumour appeared about the same size as on the previous examination, being slightly tender and adherent.

On February 7th, at operation, what appeared to be a large tubal mole was found in the left Fallopian tube. This tube lay behind the right tube and its broad ligament, being, as usual, dark purplish red in colour and slightly adherent. The entire left tube appeared extensively disorganized, and was excised. At examination an unmistakable twin pregnancy was discovered.

There was a right haematosalpinx with well-marked occlusion and infolding of the fimbriae. A large salpingostomy was performed longitudinally in the outer third of this tube, and the tubal mucosa stitched to secure eversion of the edges of the wound.

The appendix was inflamed and adherent to the posterior abdominal wall at the pelvic brim. It was removed and the abdomen was closed without drainage. The convalescence was uneventful.

On March 19th, it was thought that the right tube seemed open at 80 mm. Hg. by Rubin's test. The uterus was normal in size and position, but there was still some fullness in the left vaginal fornix. Ethidol instillation with X-ray examination showed apparent absence of patency of the remaining tube with some dilatation of its outer portion.

On April 16th the right tube was again patent at 80 mm. Hg. by Rubin's test, and a similar finding occurred again on June 12th.

The repeated tube testings noted above have been carried out both because of interest in the case and in the hope that such persufflations would exert a therapeutic effect. In view of maintained tubal patency within recent months further tube testings did not appear necessary, but if pregnancy does not follow later a further ethidol instillation may be indicated.

To summarize what is known of coincident intra-uterine and extra-uterine pregnancies, with appropriate references, we may refer to Ludwig's[1] recent paper. I now quote from it as follows:

"Combined pregnancy is to be distinguished from compound pregnancy, as in the former the intra-uterine and extra-uterine pregnancy occurs simultaneously, and in compound pregnancy the intra-uterine pregnancy is superimposed on a previously existing ectopic pregnancy which has terminated in lithopaedion formation.

"Bland in 1933 quoted authors who had collected 183 cases of compound pregnancy from 1582 to 1926, summarized 13 cases recorded to 1933, and reported one of his own, making a total of 197 cases. Mathieu reviewed the literature from 1933 to 1937, collected 32 additional cases, including a personal one, which totals 229.

"There has been considerable variance in the number of cases of combined pregnancy reviewed by equally exacting observers due to difference of opinion as to the authenticity of some cases.

"The publication of Gemmel's and Murray's exhaustive study in 1933 summarizes 217 cases from Duverney's case in 1708 to the end of 1931. Mathieu added 19 cases from 1928 to 1931 which he failed to find in the

study of Gemmel and Murray. Mathieu's study through 1936 has added 57 cases. These combined with the 217 assembled by Gemmel and Murray make a total of 274 recorded cases to the end of 1936.

"Novak in 1925 reported 32 cases collected from the literature from 1913 to 1925, including 2 cases of his own. These, added to the 244 cases assembled by Neugebauer, quoted by Novak, from 1708 to 1913, bring the total to 276, and with 57 cases reviewed by Mathieu, total 333 through 1936.

"I have reviewed 17 cases in the recent literature, and am reporting 3 original cases, which makes a total of 353 cases through 1938.

"It is interesting to note that in 20 cases reported all the mothers recovered. There were 4 pregnancies which came to term (3 intra-uterine and 1 extra-uterine), culminating in living children. One intra-uterine pregnancy terminated at 8 months, another continued through 6.5 months with the probability of having continued to term."

In the same issue of the American journal, Torpin[2] records a case of simultaneous bilateral tubal pregnancy, and supplies the details. Within recent months several other reviews of multiple pregnancy in the Fallopian tubes have appeared in the American literature, but they are not included here as they do not add any further new facts.

In this particular case it would seem that both Fallopian tubes had been inflamed before pregnancy occurred, possibly secondary to the appendicitis. It may also be suggested that whereas the left tube had either escaped without occlusion of its fimbrial end, or this end had subsequently overcome any plastic reaction and allowed the ovum or ova to enter, the right tube had either suffered more severely or had not recovered as rapidly. It is also quite possible that the right tube may have been open and normal when either of the pregnancies began but later became occluded either as a result of aseptic irritation from regurgitated blood from the intra-uterine abortion or by persistent leakage from the tube of the opposite side into the uterine cavity before the intra-uterine abortion took place.

REFERENCES.

1. Ludwig, D. B. *Amer. Journ. Obstet. and Gynecol.*, 1940, xxxix, 2, 341.
2. Torpin, R. *Amer. Journ. Obstet. and Gynecol.*, 1940, xxxix, 2, 345.

Royal College of Obstetricians and Gynaecologists

The Quarterly Meeting of the Council was held in the College House on Saturday, October 26, 1940, with the President, Professor W. Fletcher Shaw, in the Chair.

The following were admitted *in absentia* to the Membership of the College:

Anderson, Anthony Francis, Edinburgh.
Apthorp, John Owen East, Cape Town.
Dingle, William Thomas, Canada.
Fraser, Donald Blake, London.
Lester, George Stephen, Walsall.
Liggett, Samuel Wilberforce, London.
Murdoch, Robin, R.A.M.C.
O'Gorman, Frank Joseph Patrick, Sheffield.
Rendle-Short, Coralie Winifrede, Bristol.
Thomas, Ivor Elwyn Joseph, Tunbridge Wells.
Watt, Lindsay Oswald, Canada.
Way, Stanley, Newcastle.
Deacon, Arthur Leonard, London.

The examinations for the Membership and for the Diploma continue to be held.

The Library and Museum of the College are open daily except Saturdays.

Examination for the Diploma, October 1940.

The following candidates have satisfied the Examiners for the D.R.C.O.G.:

Balfour, Harold Ivor Collingwood, West Worthing.
Corbett, Henry Vincent, Liverpool.
Doberman, Henry, Middlesbrough.
Edmonds, Ruth, Leeds.
Farquhar, John Burns, Birmingham.
Gaudin, Melvin Lloyd, Canada.
Grimshaw, Clement, Perth.
Martin, Doreen Martin, Preston.
McCann, Mary Clare Josephine, London.
Pearson, Alexander Frederick, Salford.
Swan, Henry Peter, London.
White-Jones, Robert Howel, Liverpool.

BOOK REVIEWS

"Obstetrics and Gynaecology, 1940." Edited by FRED. L. ADAIR, M.D. (Henry Kimpton Ltd.) 2 vols. 2010 pages.

THIS work consists of two volumes, each containing about 1,000 pages. It is profusely illustrated, and most of the illustrations and diagrams are excellent. It is edited by Professor Fred. L. Adair, Chief of Service, the Chicago Lying-in Hospital. There are 63 contributors, most of whom are, or have been, associated with the Department of Obstetrics and Gynaecology of the University of Chicago, and with the Staff of the Chicago Lying-in Hospital.

The work is a presentation of the combined judgment of the contributors on the various matters contained therein, in both obstetrics and gynaecology.

It is pointed out by the Editor that it is intended to present the *educational essentials* rather than the comprehensive details of the speciality of obstetrics and gynaecology.

It is also stated that, "There is a growing tendency to combine obstetrics and gynaecology under one leadership for the purpose of improved service, teaching and research". "In medical schools such duplication of effort, repetition, omissions, lack of co-ordination of material, could be avoided if the subjects were sometimes taught collaterally by the same teachers under one plan of instruction."

These two statements may explain the reason for the way in which such important subjects as occipito-posterior presentation, premature placental detachment and a few others, appear to be rather scantily dealt with, and also will provide an excuse for the very peculiar arrangement of the two volumes.

The majority of textbooks are arranged so as to enable the student of obstetrics to get a clear-cut picture of the normal woman, normal pregnancy, normal labour, normal puerperium, and normal baby. It is hoped that by this arrangement the student, having to some extent mastered the normal, will be able more readily to recognize the abnormal when he meets it.

The work under review changes all this—in fact it is revolutionary.

Obstetrics and gynaecology are intermingled to a bewildering degree. For instance in the first 20 chapters there are only 5 dealing directly with obstetrics. The intervening chapters deal with such subjects as *Malignant Disease of the Female Genitalia, Classification of Tumours, History of the Development of Gynaecology, Maternal and Foetal Mortality, Menopausal Conditions, Marital Physiology and Pathology, Sterility and Infertility, Limitation of Human Reproduction* (*Contraception.*)

By the time the student of obstetrics has reached this stage of his

reading, I feel sure his conception of the normal woman will have become seriously clouded.

While it must be agreed that there is a very close association between obstetrics and gynaecology, there is still a line of demarcation, however ill defined. What is the relation between placenta praevia and gynaecology, and what has the treatment of malignant disease of the genitalia to do with obstetrics?

To try to teach these two subjects together would seem to make it very difficult for the student.

The various subjects both in obstetrics and gynaecology throughout the work are well described and, for the most part, well illustrated.

The mechanism of normal labour is beautifully illustrated. This is followed at once by abnormal mechanisms, such as brow, face, shoulder and caudal presentations. The method of delivery in the latter is fully illustrated. It is not, however, until much later that a full description of breech delivery is given. Before we get to this we have to deal with natural labour, neonatal care, identification of newborn, physiology, management and pathology of the third stage of labour, obstetrics in the home and emergency management. Under this latter heading are included placenta praevia and premature placental detachment and their treatment. Neither of these conditions has so far been described. How the student can be expected to comprehend the treatment of the two conditions described before he has been taught what the conditions really are, is rather difficult to understand.

The description of the mechanism by which the placenta is separated is open to argument. The statement that "except in cases of premature placental detachment the placenta maintains its attachment until after delivery of the foetus" cannot be accepted without proof. The importance of retraction is not stressed.

The usual signs of the placenta having been expelled from the uterus are referred to as signs of the complete detachment of the placenta. The placenta may have been, and very often is, separated long before these signs have arisen. The important thing to remember is that if the placenta has separated it is no longer of use to the infant.

The description of *Delivery in the Home* is very good, and should prove of great help to the young doctor starting practice.

Placenta praevia and premature detachment of the placenta are somewhat lightly dealt with. The usual methods of treatment are described. The insertion of Vorhees's bag seems in favour, and plugging of the vagina is also mentioned.

Having already dealt with the mechanism of caudal presentation and the method of delivery, we are now treated to a long chapter dealing with the aetiology, diagnosis and treatment. There is nothing new in this chapter. The teaching of the past 40 years is duly passed on. Few obstetricians will agree with the statement made on page 878, Vol. I, that "the breech never enters the pelvic inlet prior to the onset of labour," and again on page 867, Vol. I, that "the second stage is usually brief". The

usual methods of delivering the after-coming head are described. No distinction is made between fundal pressure and suprapubic pressure. On page 889, Vol. I, the manœuvres to get the head through the brim are described, yet on page 882, Vol. I, it is stated that when the shoulders are born the head is in the pelvis. Forceps for the delivery of the after-coming head seems to be in favour.

Having already read about placenta praevia and accidental haemorrhage and their treatment, we now come to an extensive article on these two subjects. The final judgment so far as treatment of placenta praevia is concerned is expressed in the two paragraphs on page 944, Vol. I. If the placenta is complete, Caesarean section is the procedure of choice, provided there has not been much examination, etc. If the placenta is incomplete the baby should be delivered *per vaginam*. Caesarean section should be done only when delivery from below is too dangerous for the mother and foetus.

Post-partum haemorrhage is described as an abnormal amount of bleeding during the third stage and the immediate post-partum or fourth stage. This fourth stage is not described. It seems a pity that a sharp line of demarcation is not drawn between third stage bleeding and post-partum bleeding. The treatment of these two conditions is essentially different.

Post-partum care is well described, particularly that section dealing with puerperal infection. Isolation is advised. The various forms of treatment both new and old are well described.

A very extensive section of Vol. II is devoted to paediatrics. The subject-matter in this section can have but a passing interest to the obstetrician or gynaecologist or student.

Malignant disease of the female genitalia is very well described. The treatment does not differ from that usually carried out on this side of the Atlantic. Radium and X-rays with surgical measures are employed in selected cases. Vulval carcinoma is treated by radium and surgical measures. The latter is carried out in two stages, (1) excision of vulva, and (2) excision of inguinal glands at a later date.

Tumours of the ovary are nicely dealt with. The suggested classification seems much simpler than that which appears in recent literature and should appeal to the student.

Adenomyosis and endometriosis are described. Nothing new is added. The statement that "endometriosis is a gynaecological condition too seldom recognized before operation" about describes the present situation in regard to the condition.

Relaxations of the female genitalia, in other words prolapse, uterine, utero-vaginal and vaginal, are dealt with. This subject seems poorly described. There does not seem to be as much importance attached to this condition as it deserves considering that 75 per cent of a gynaecologist's work consists in dealing with these conditions. The surgical treatment advised and described seem to lie between (1) vaginal hysterectomy and a plastic vaginal operation, or (2) vaginal plastic operation plus an abdominal operation on the round ligaments. The round ligaments are

given an importance in these operations for the cure of prolapse not usually accorded thereto in English literature.

Venereal disease, its diagnosis and treatment, is extensively dealt with and should prove of very great interest to the specialists in this condition. Despite the fact that the incidence of genital tuberculosis in the female is so very small, this subject receives special attention. The greater portion of this section lies more in the realm of the physician than in that of the gynaecologist or obstetrician. The association of pulmonary tuberculosis with pregnancy is dealt with on modern lines. There is no new information.

Infections of the genitalia, apart from venereal disease, are shortly dealt with. Leucorrhoea is described as a "whitish or yellowish discharge" which originates at or above the vaginal level. There are no less than 45 conditions mentioned which may produce leucorrhoea.

Trichomoniasis receives special attention. It is interesting to note that doubt is cast on the pathogenicity of these protozoa and also their source. It is stated that trichomoniasis without vulval or vaginal irritation occurs in from 5 to 15 per cent of pregnant and non-pregnant patients. Lactose seems to be the main treatment advised.

Endocervicitis. This is a very good chapter, particularly in regard to the pathology. The treatment suggested is cauterization and office treatment. Excision of the eroded area, it is stated, may lead to a cure. In view of the pathology described it seems a little unscientific to advise the removal of cervical polypus by torsion of the pedicle.

Section III, Vol. II. This section is mostly taken up with medical and surgical conditions which may be associated with the pregnant state. The chief conditions which have an interest for the obstetrician are chronic renal disease and cardiac disease. Why chronic renal disease should be divorced from the chapter dealing with toxaemias of pregnancy seems strange.

Cardiac cases are divided into three classes:

(1) Organic heart disease and able to carry on ordinary physical activities without discomfort.

(2) Organic heart disease and unable to carry on ordinary physical activity.

(3) Organic heart disease and marked signs of decompensation.

The dividing line between 2 and 3 is very thin.

Treatment. Groups (1) *and* (2). Rest for one or two weeks before labour is advised and the second stage should be shortened as much as possible.

Group (3). Caesarean section under local anaesthesia is advocated.

There is a long article on diabetes mellitus which is mainly of medical interest.

Having already dealt with the abnormal pelvis in Vol. I, we are now again treated to a long article on deformities of the pelvis due to regional diseases, such as tuberculosis of the hip-joint, congenital dislocation of

the hip, fracture of the pelvis, etc. One might reasonably expect to find these conditions included under the study of the abnormal pelvis.

One of the most common conditions requiring the attention of the obstetrician is pyelitis, either in the pregnant or puerperal patient. In spite of this, this important condition is dealt with only in the final chapters of Vol. II. The article is very good and agrees with the teaching in most English clinics.

X-rays and pregnancy are dealt with *in extenso*. This section is highly technical and can be appreciated only by the X-ray specialist. It is unfortunate that the obstetrician cannot always be an expert in X-rays. He has, therefore, to rely upon reports to a great extent. The experienced obstetrician can, however, form a very good idea as to the possible conduct of any given labour if he is presented with a good film. In any case the obstetrician and the X-ray expert make a very good combination.

Post-operative Treatment. Gynaecological cases. In common with most English textbooks, morphia in some form is advised in order to relieve pain following operation. The fact that post-operative discomfort arises in most cases from abdominal distension is quite lost sight of. The giving of morphia following operation engenders the distension by causing stasis of the bowel.

The section on anaesthetics both in obstetrics and gynaecology is very interesting and very helpful.

Caesarean section is dealt with in a long section; the history of the procedure is given from good old Julius Caesar to the present day.

The general mortality is stated to be between 6 and 10 per cent, which seems rather high.

Hysterectomy is next described but not illustrated. Comparison is drawn between the values, complications and mortality of the various types, abdominal, sub-total, complete and vaginal.

The final chapters of the second volume are devoted to *Version*, *Forceps*, and *Destructive Operations*.

It must seem strange to the British reader that two of the most common operations carried out in obstetrics, version and the application of the forceps, should be delegated to the final chapters of a work containing 2010 pages.

Version in its various forms is described. The foetal mortality following the operation is stated to be between 4 and 5 per cent. We do not think that it is generally appreciated that such a high foetal mortality is associated with such a manœuvre as external version. It is usually looked upon as such a simple operation that it is more often than not delegated to the junior staff of most hospitals.

Forceps, History of, various types, indications for application of and technique are all well described and illustrated. Under the heading *Forceps* a study of occipito-posterior presentation and its treatment is included. Considering that this condition is responsible for a very high incidence of meddlesome midwifery in general practice, it seems a little strange that it should be included under *Forceps Delivery* instead of

alongside malpositions arising as a result of varying degrees of deflection of the head. It is stated that in only rare instances will it be found impossible to rotate the head anteriorly. Such cases necessitate delivery with the face towards the symphysis, and this procedure almost invariably results in extensive trauma to the vagina and the pelvic floor.

This teaching is very ancient and has produced a condition of mind in most obstetricians that it is a sin and crime to deliver a posterior position face to pubes. Compare the amount of handling necessary to rotate the head and then apply forceps and that of simply applying the forceps. Delivery with the face to pubes entails much less manipulation and therefore less risk of trauma. The torn perinaeum can be avoided in many instances by a well-chosen episiotomy. In any case the torn perinaeum can be repaired at once, and in the majority of cases heals by primary union. The mother will be more grateful for a living infant and a torn perinaeum than a dead baby and a torn perinaeum into the bargain.

There is no shame attached to the delivery of a head face to pubes. If the truth were known, probably 99.5 per cent of expert obstetricians have delivered a face to pubes when they thought they were dealing with an occipito-anterior.

Inlet forceps, or high forceps, is recognized as a method of treatment. In expert hands the operation may succeed on occasions, but in the hands of the inexpert it becomes almost a criminal proceeding.

Duhrssen's Incisions. This operation is described and illustrated. It is pointed out that the operation is for specially trained practitioners only, to be carried out in suitable environment such as a well-equipped maternity hospital.

This operation was carried out in 592 cases in the Chicago Clinic. In 84 per cent of the cases the indications for the operation were occipito-posterior and transverse positions of the head. The high incidence of this very dangerous operation will appear strange to the British reader.

The remaining pages of Vol. II are taken up with a description of the various destructive operations upon the child. There is an appendix which is full of all sorts of odds and ends of information.

This work, by reason of its peculiar arrangement, will be read with interest by the senior obstetricians and gynaecologists, particularly those engaged in teaching.

The student will find it difficult, not only because of the arrangement, but because of close association between the normal and the abnormal. He no sooner gets a mental picture of the normal than it becomes clouded by the abnormal and many other subjects which have only a remote association with pregnancy. Another defect appears and that is that some very important subjects appear to be dealt with piecemeal, viz., placenta praevia, breech, occipito-posterior. Information about these subjects appear in various chapters scattered throughout both volumes. The work cannot be looked upon as a book of reference by the general practitioner because of the fact that in most of the subjects only general principles are described.

J. W. B.

"Foetal and Neonatal Death," by EDITH L. POTTER, M.D., PH.D., and FRED. L. ADAIR, M.D. (U.S.A., University of Chicago Press; Great Britain and Ireland, Cambridge University Press.) March, 1940. 198 pages. Price, 9/- net.

"A survey of the incidence, etiology and anatomic manifestations of the conditions producing death of the foetus *in utero* and the infant in the early days of life." This sub-title adequately describes the scope of the book.

It includes statistics from the Chicago Lying-in Hospital and from the literature, and some useful tables giving particulars such as weight, size and ossification at different stages of development of the foetus. The best chapters are those dealing with the appearances of the normal foetus and the technique of post-mortem examination. These are clear and concise, and should prove of the utmost value to those called upon to perform autopsies.

In order to keep the survey within the scope of a small book, the authors have chosen to mention nearly all the known conditions causing foetal and infant death without describing any in great detail. This, at times, conveys the impression of incompleteness, but is compensated for by lists of references at the end of each chapter.

The description of erythroblastosis foetalis, lung pathology, and the discussion on asphyxia and prematurity as causes of death deserve special mention. References to "haemorrhagic disease" and pemphigus are disappointing, and it is a pity that so little space is devoted to placental pathology when in an earlier chapter the importance of examining the placenta as well as the foetus is rightly emphasized.

Very little adverse criticism is possible, however, for it is clear that the authors have made no attempt to write a book of reference or even a textbook. This book has a moral, and it constitutes an appeal to all those concerned with obstetrics and pediatrics to make the effort required to reduce the present high rate of antenatal and neonatal death. As the authors point out, this mortality rate could immediately be reduced by one-third and result in the saving of 55,000 lives per annum in the United States, if only present-day knowledge were put into universal practice. They enter a plea for the standardization of statistics, and make suggestions as to classification. They appeal most of all for routine autopsy before certification of the cause of death, for more careful diagnosis and for more accurate records.

By such sentences as the following: "Prematurity cannot be considered a cause of death in a still-born foetus. Regardless of the degree of prematurity, unless some pathologic condition has developed, the foetus should be born alive even though an extra-uterine existence cannot be established", the book has the effect of stimulating the reader to a more logical and scientific approach to the subject.

The wrapper states that it was written for doctors, interns, nurses and

students, but it will well repay the attention of specialist obstetricians and pediatricians.

This latest publication from the Chicago Lying-in Hospital is unpretentious, well written and easy to read. It conveys a message to all those engaged in obstetric practice, and by directing attention to the problem of foetal and infant mortality and by indicating the lines on which everyone can play their part in its investigation, this book should play an important role in reducing the present high death-rate among the unborn and newly-born.

T. N. A. Jeffcoate.

"The Anatomy of the Female Pelvis," by F. A. MAGUIRE, *C.M.G.*, *D.S.O.*, M.D., Ch.M., F.R.C.S., F.R.A.C.S., F.R.C.O.G. (Sydney: Angus and Robertson Ltd.) Price, 10*s*. 6*d*.

This book makes the anatomy of the female pelvis a simple and interesting matter. It is most clearly written, and even such subjects as the pelvic fascia are described and explained in such clear terms that anyone should be able to obtain a clear mental picture.

The illustrations are drawings by Mr. D. J. Farrell from sections and dissections, and are numerous and excellent. They are largely self-explanatory but are made even clearer by numbers allotted to groups of structures in the pelvis, the same number being adhered to throughout the book. Thus in all the illustrations in which it appears, the internal pudendal artery is No. 59. Its branches are Nos. 59, *a*, *b*, *c*, etc.

It is interesting for the reviewer to observe in this book the struggle between the anatomist and the gynaecologist that is going on in the author. The gynaecologist is clearly on top when the close relation between the ureter and the ovarian vessels in the infundibulo-pelvic fold as it crosses the brim of the pelvis, is pointed out. The same applies in the description of the vascularity of the lateral vaginal angle, and particularly in those two splendid chapters on "Applied Anatomy" and "The Physical Examination."

But the anatomist comes into his own in such things as the detailed description of vascular anastomoses and venous plexuses. Also in the belittling of the utero-sacral ligament as a support of the uterus and in the rather inadequate description of the pelvic cellular tissue. In this section it is not made clear that the so-called Mackendrodt's ligament is the same thing as the connective tissue sheaths of arteries, nerves, etc., upon which the author lays stress under a different heading. It may also be advanced as an adverse criticism that the sympathetic nerve supply of the pelvic organs is deserving, in a modern book, of fuller description. But, generally speaking, this small volume of anatomy is lucid, helpful and easily read.

L. W.

Review of Current Literature

Director: FREDERICK ROQUES, M.A., M.D., M.Chir. (Cantab.), F.R.C.S., F.R.C.O.G.

THIS Review contains the lists of contents and abstracts of the more important articles from the journals with which the "Journal of Obstetrics and Gynaecology of the British Empire" exchanges.

The Review of Current Literature has kept the readers of the Journal in touch with current literature throughout the world; owing to the war many journals with which the *Journal of Obstetrics and Gynaecology* previously exchanged are no longer received. At the end of the year an Index of all the subjects contained in the articles of the journals reviewed is printed. Arrangements are also made to include abstracts of important articles on border-line subjects, such as Physiology, Biology, and Biochemistry.

LIST OF ABSTRACTORS

J. LYLE CAMERON, F.R.C.S.; W. E. CROWTHER, M.B.; R. H. B. ADAMSON, M.D.; B. JEAFFRESON, F.R.C.S.; P. MALPAS, F.R.C.S.; T. N. A. JEFFCOATE, F.R.C.S.; MEAVE KENNY, F.R.C.S.; JANE H. FILSHILL.

The Lancet

4th May, 1940.

*Death in the first month and the first year: (1), Neonatal deaths. Charles McNeil.

11th May, 1940.

*Death in the first month and the first year: (2), Feeding in the first month. Charles McNeil.

18th May, 1940.

Death in the first month and the first year: (3), Infant death-rates at home and abroad. Charles McNeil.

*Response of non-gravid human uterus to posterior-pituitary extract, and its fractions, oxytocin and vasopressin. A. McLellan.

Rupture of a branch of the splenic artery associated with pregnancy. Douglas MacLeod and Timothy Maurice.

1st June, 1940.

Death in the first month and the first year: (4), Towards better control. Charles McNeil.

8th June, 1940.

*Missed abortion and missed labour. T. N. A. Jeffcoate.

DEATH IN THE FIRST MONTH AND THE FIRST YEAR.

1. Neonatal Deaths.

McNeil reviews the cause of death in the first two weeks of life. The fall in the neonatal death-rate has not been nearly so great as the fall in the infant death-rate for the first year, and the author is of the opinion that an improvement could be obtained. Broadly, these deaths are due to morbid conditions in the mother during pregnancy, to the risks of birth, and to diseases developing in the first week or two after birth.

In this series the still-birth rate was 79 per 1,000 viable births, and prematurity, 68 cases, played the most important part. The neonatal death-rate was 59 per 1,000 live-births and prematurity accounted for more than half of these. The standard of prematurity used in this series was a weight of less than 5½ pounds. This cause of death could be decreased by improved antenatal care and by an improvement in the nursing and feeding of the premature babies.

The actual causes of these neonatal deaths fell into three main groups of about equal size: (*a*) intracranial haemorrhage, (*b*) infection, and (*c*) a miscellaneous group, including congenital defects, asphyxia, etc. Intracranial haemorrhage was the biggest single factor. There was a definitely greater liability of premature infants to this accident (28 to 12) and a decrease of premature births would definitely lessen this cause of death considerably. The author found that in the mature babies the site of the bleeding was subdural in most cases, while in the premature babies it was either subarachnoid or intraventricular.

In this series the part played by post-natal infection as a cause of death was high. Of these 43 fatal cases pneumonia accounted for 25, meningitis for 7, septicaemia for 7; in the remaining four cases death was due to gastro-enteritis and pyelo-nephritis. The author stresses the importance of a high and strict standard of antiseptic routine among the medical and nursing staffs. He quotes Macgregor, who found, during her investigations, that many cases of pneumonia developing in hospital are due to droplet infection of the baby's naso-pharynx from the air. Therefore the author points out that the key to the solution of infection of the newborn is the trained and conscientious nurse who is taught the manifold sources and channels of infection and is thoroughly drilled in the practical technique of guarding the baby against them.

2. Feeding in the First Month.

In the first fortnight after birth the antenatal and natal causes of death have spent their force; after this, mismanagement of feeding in the first month and afterwards is the new lethal agent.

McNeil states that throughout the country medical and nursing control of dietetics is poorly managed. This so disturbs and lowers nutrition that the gate to infection is opened wide. He explains how quickly the digestive processes of the baby have to get into full working order and how important it is to feed the child on natural breast-milk; successful breast-feeding gives the best results in nutrition, and provides the strongest guard against every kind of infection. He implores the medical and nursing profession to guard against unnecessary weaning, especially for such reasons as vomiting or supposed poor quality of the milk. Unnecessary weaning commonly takes place in the second half of the first month when the mother again takes up the full load of household duties.

McNeil is of the opinion that the three processes, lactation, suckling, and digestion, must be taught in detail to all students, both medical and nursing, with special training in suckling. If disorders of these three processes are located and understood, most of them can be overcome; if they are mishandled, the life of the baby may easily be endangered.

Response of non-Gravid Human Uterus to Posterior-Pituitary Extract and its Fractions, Oxytocin and Vasopressin.

The authors tested the response of uterine contractions in a series of 43 normal women. The movements of the uterus were recorded by introducing a small rubber bag, filled with water, into the uterus and by registering the changes in volume. They found that the uterus responded to posterior-pituitary extract immediately before and during menstruation and in the early interval part of the cycle. Oxytocin (pitocin) did not have any effect on contraction, although a slight response was obtained during the menstrual phase in two instances after the administration of 0.4 units. On the other hand, vasopressin (pitressin) caused the non-gravid uterus to contract in every case throughout the cycle.

Missed Abortion and Missed Labour.

Jeffcoate reports a series of 55 patients treated with oestrogenic substances for the evacuation of dead products of conception from the uterine cavity. The theory of this mode of treatment resulted from the findings of Frank in 1933, who showed that intra-uterine death of the foetus is accompanied by a fall in the amount of free oestrogens in the blood-stream. This change in the oestrogen content of the blood is dependent upon an alteration in placental function rather than the actual death of the foetus. This treatment increases the sensitivity and activity of the uterine muscle so that it will more readily react to oxytocic agents.

The author's technique is to give 2 mg. of oestradiol benzoate every eight hours for seven or eight days. If the uterus has not evacuated its contents by the fifth day, quinine hydrochloride, gr. 10, is given each hour for three doses and this is followed by four injections of 0.5 c.c. of pituitary extract at intervals of one hour. This treatment is repeated on the eighth day if the uterus is not emptied. Of this series, 14 were given oestrone

or oestrone benzoate, 30 were given oestradiol benzoate, and 11 were given stilboestrol. In 29 of the successful cases nothing but oestrogen was administered, but in the remainder oxytocic drugs had to be given. The author is of the opinion that the ease with which hormone induction may be brought about varies directly with the duration of the pregnancy before the death of the foetus, and inversely with the length of time during which the products of conception have been dead.

British Medical Journal

Vol. i, May 18th, 1940.

*Axial rotation of the pregnant uterus. G. Shedden Adam.

Vol. i, May 25th, 1940.

*Effect of intrapartum and neonatal administration of synthetic vitamin K analogues on the newborn. A. I. S. Macpherson, E. McCallum, W. F. T. Haultain.

*Treatment of haemorrhage in the newborn. Editorial.

Minor surgery of the newborn. Denis Browne.

Vol. i, June 1st, 1940.

*Vitamin E and habitual abortion. A. L. Bacharach.

Vol. i, June 8th, 1940.

The circulation in relation to shock. R. J. S. McDowall.

Vol. i, June 15th, 1940.

*The sulphonamide treatment of gonorrhoea. R. C. L. Batchelor, R. Lees, G. M. Thomson.

Vol. i, June 22nd, 1940.

Progesterone and vitamin E treatment during pregnancy: case report. H. MacCallum.

Vol. i, June 29th, 1940.

*Volume and rate in blood-transfusion for the relief of anaemia. H. L. Marriott and A. Kerwick.

*Plasma transfusions in the treatment of haemorrhage. H. J. Brennan.

Vol. ii, July 6th, 1940.

*Reactions from transfusions of preserved blood. Elmer L. DeGowin and R. C. Hardin.

*Chemotherapy for gonococcal infections in women and children. Mary Foffett.

*Treatment of the impacted shoulder. J. A. Waterman.

Axial Rotation of the Pregnant Uterus.

Lesions causing acute abdominal pain with rigidity and vomiting in pregnancy are diverse. It is essential to determine whether the lesion is intra-uterine or extra-uterine. It is difficult to distinguish torsion of the uterus from concealed accidental haemorrhage. Whilst minor degrees of torsion are common, it is rare to meet it of such degree and persistence as to require laparotomy.

The case of a primigravida aged 30 is described. After a normal pregnancy she developed abdominal pain and uterine tenderness at the thirty-third week. The onset was gradual, and vomiting and faintness supervened. Symptoms persisted in spite of treatment with morphia, and four days later the membranes were ruptured artificially—a diagnosis of abruptio placentae having been made. Pain and tenderness increased but labour did not ensue, and the foetal heart was no longer audible. Laparotomy revealed a clockwise rotation of the uterus through 90°, the uterus being tense but not congested. Classical Caesarean section was carried out after eventration of the uterus and correction of the torsion. There was no retro-placental haemorrhage. The baby was born alive, but died in 12 hours from prematurity. The patient made a good recovery in spite of a local saprophytic uterine infection.

Possible aetiological factors in torsion of the uterus are the softening of the lower segment, foetal movements, and posture. The differential diagnosis is from abruptio placentae, tonic uterine contraction, necrobiosis in a fibroid, acute hydramnios, and acute appendicitis.

A possible line of treatment is to correct the rotation of the uterus at operation and then allow natural delivery of the child. This procedure involves the risk of recurrence of the displacement.

Effect of Intrapartum and Neonatal Administration of Synthetic Vitamin K Analogues on the Newborn.

The tendency to haemorrhage in the newborn has now been shown to be related to a prolonged coagulation time and low prothrombin level in the blood. Icterus gravis and hydrops congenitus are also characterized by hypothrombinaemia. It is possible that prothrombin deficiency influences the extent and incidence of intracranial haemorrhage following birth trauma.

In clinical experiments the prothrombin index was deduced by measuring the coagulation time and expressing this as a percentage of the coagulation time for a normal adult. The prothrombin index was estimated during the first week of life in 54 babies. The results showed considerable variations in the same individual, but in general demonstrated a fall in the prothrombin index which reaches its lowest level 36 to 44 hours after birth. About the fifth day it rises sharply to 75 per cent, and thereafter rises slowly to normal. The level is the same in all babies at birth, but the subsequent fall is greater after difficult deliveries, irrespective of the type of feeding. The fall is not influenced by the length of labour or prematurity.

Maternal bloods examined usually showed a figure above 75 per cent

except in two cases of pregnancy toxaemia. Blood from the umbilical cord has a prothrombin index of 15 per cent to 20 per cent below the maternal.

The vitamin K analogues administered orally to babies were: (1), 2 methyl-1: 4 naphthoquinone in doses of 2.5 mg. 2 to 4 times immediately before feeds; (2), Diacetyl-2-methyl-1 : 4 naphthoquinone, in one dose of 10 mg. before a feed.

The second is less irritating and unpleasant than the first. If given in the first 24 hours the prothrombin index is raised to 80 to 90 per cent and maintained during the first few days of life.

In 31 cases the vitamin K analogue was given to the mother in labour, the optimal time being 12 to 4 hours before delivery. Not more than 50 mg. orally, or 15 mg. intramuscularly, is necessary. The effect on the prothrombin index of the baby is equally good with antenatal as with postnatal therapy. It has no effect on labour or the placental circulation.

Sixteen cases of intracranial birth injury were also treated. The prothrombin level falls unusually low in these cases, and, coinciding with the fall, the babies show an exacerbation of the signs of cerebral irritation. This may be due to a new oozing of blood. Such secondary symptoms respond well to vitamin K therapy.

The possible causes of vitamin K deficiency in the newborn are the low vitamin K content of milk, the absence from the large bowel of bacteria capable of synthesizing the vitamin, and the bile may not be suitable for optimal absorption.

The birth of a child with adequate amounts of vitamin K and prothrombin in circulation is desirable, and the routine administration of this substance to women in labour may become a practice. It should be given especially in the presence of (i) toxaemia of pregnancy, (ii) prematurity, (iii) difficult delivery, (iv) artificial feeding, (v) symptoms of cerebral irritation, (vi) haemorrhagic disease, icterus gravis and anaema, (vii) when operation on the newborn is necessary.

Treatment of Haemorrhage in the Newborn.

The fall in the prothrombin level of the blood in the early days of life is now agreed by all workers. Vitamin K and its analogues counteract this fall, and they are of the utmost value in haemorrhagic disease of the newborn.

With regard to intracranial injury, vitamin K will not control bleeding from a torn tentorium. In those cases showing a late onset of symptoms, there may be a secondary oozing due to a haemorrhagic diathesis, and vitamin K might be helpful. Further evidence is required, however, before the claims of the Edinburgh workers (vide supra) can be accepted.

Icterus gravis, however, is different from haemorrhagic disease of the newborn, and there is no reason to believe that it can be influenced by vitamin K. Injection of whole blood or blood-transfusion is the treatment of choice. When it appears in successive children of the same parents, it may be prevented by liver therapy during the last three months of pregnancy.

Vitamin E and Habitual Abortion.

The treatment of habitual abortion by vitamin E results in 75 per cent of live births. However, it is difficult to control these clinical trials. Malpas, in 1938, from his own and reported statistics, calculated the chances of live birth if such cases are untreated, and found them to be 62 per cent after two, 27 per cent after three, and 6 per cent after four successive abortions.

Further inquiry into the statistics of Malpas and other writers indicates that the chances of live birth without treatment are not so good as these figures imply.

Vitamin E is essential for normal reproduction in mice and rats, and is necessary for the production of hen's eggs. It has been successfully used as a therapeutic agent in cows and sows, but it is of little importance to reproduction in goats, sheep, and rabbits.

For woman, no definite conclusions can yet be drawn, but statistics do show that vitamin E is of therapeutic value.

The Sulphonamide Treatment of Gonorrhoea.

Male and female cases of gonorrhoea were treated with sulphonilamide and sulphapyridine.

There were 129 cases of the disease in women, and the average dose employed was 44 grammes of sulphonilamide during 2 weeks or 13.5 grammes of sulphapyridine during one week repeated after one week's interval. Although 76 per cent of sulphonilamide gives a slightly higher percentage of cures than does 60.9 per cent sulphapyridine the latter ensures a more rapid control of contagion and relief of symptoms; it also has a lower incidence of toxic manifestations.

There was a high proportion of defaulters, 24 per cent with sulphonilamide and 39 per cent with sulphapyridine.

Complications such as Bartholin's abscess and salpingitis occurring during treatment were few. Drug resistance, a personal idiosyncrasy, was encountered in 18 per cent of cases treated with sulphonilamide and 5 per cent with sulphapyridine. Such resistance is sometimes the result of inadequate dosage. Only two cases showed a late relapse.

Uleron is less potent than sulphapyridine and equal in value to sulphonilamide, but is more toxic. Albucid has low toxicity, but is only feebly active against the gonococcus. M.541 is of no value in the treatment of gonorrhoea.

Volume and Rate in Blood-transfusion for the Relief of Anaemia.

The conclusions are based on a series of 194 drip-transfusions for anaemia uncomplicated by acute haemorrhage.

Anaemia is haemoglobin deficiency, and the essential purpose of transfusion is to administer haemoglobin. Transfusion should not be used for those cases in which the anaemia can be treated by ordinary medical measures. It is indicated when, (1) the anaemia reaches a dangerously low level: less than 25 per cent. In such cases the level should be raised to 45 per cent. (2) When anaemia is complicated by the need for surgical treatment. The

level should then be raised to 80 per cent. (3) When the patient's recovery must be expedited for special reasons. Restoration to 100 per cent should then be the aim. (4) When the anaemia is aplastic in type and will not respond to medical measures. The haemoglobin level should be raised to 60 to 80 per cent in such cases. (5) When the anaemia is the result of septic and infective conditions. The level should then be raised to 100 per cent.

The volume of blood required in any case depends on the patient's weight and the desired level of haemoglobin. It may be calculated as follows: (Per cent rise in haemoglobin required ÷ 100) × Patient's normal blood-volume in cubic centimetres. The normal blood-volume is approximately 40 c.c. per pound of body weight.

In practice, the administration of one pint of blood raises the haemoglobin level by 10 per cent. If a rise of more than 33 per cent is required, it is better to give two transfusions with an interval of two days between them. Fresh blood is advised, for red cells which have been stored for longer than one week quickly disappear from the recipient's circulation.

The danger of transfusing large quantities is cardiac embarrassment. Chronic anaemia enfeebles the cardiac muscle. This danger is avoided by slow administration.

In this series of cases, adults received an average of 2,039 c.c. of blood, 21 receiving over 3,000 c.c. Distress was seen in five of the early cases, and one patient died owing to lack of adequate supervision. The average duration of the transfusion was 27 hours, that is, 84 c.c. per hour in adults.

The rate of administration should never exceed 1 c.c. per hour per pound of body weight, and in cases of severe anaemia and cachexia, half this rate is advisable. The rate of transfusion should be kept constant and never speeded up even for short periods. Careful watch for signs of cardiac embarrassment is essential. Slow drip-transfusion also has the advantage of diminishing the incidence and intensity of reactions.

The prevalent practice of giving one pint of blood in half an hour is irrational, and dosage and speed of administration should be prescribed for each case individually.

Plasma Transfusions in the Treatment of Haemorrhage.

The blood changes during 130 neuro-surgical and 56 general surgical operations were studied. As a result of haemorrhage, the red cells increase in size often as much as 30 to 50 per cent. This swelling is possibly due to entrance into the blood-stream of tissue fluids of low osmotic pressure. Also, after haemorrhage, many of the red cells disappear from circulation, probably into the muscle capillaries. With the lowering of blood-pressure and increase in size of the corpuscles, capillary stasis occurs, and as many as 20 per cent of the red cells may be temporarily out of circulation. The administration of plasma, by raising the osmotic pressure, should cause the red cells to return to a normal size and be restored to circulation. Such restoration is equivalent in many cases to a transfusion of 1,000 c.c. of blood.

Plasma transfusion was used in 21 cases, and it was found as useful for haemorrhage as for shock. Determination of the blood groups is unnecessary, the plasma can be stored for months without elaborate refrigeration. For administration, the plasma was mixed with an equal quantity of Baxter saline and given rapidly, at the rate of 500 c.c. in 20 to 35 minutes. Serial blood-counts showed an increase in the number of red cells in circulation and a return to normal in their size.

Preliminary results indicate that plasma transfusion may replace blood-transfusion, and there may even be a place for artificial plasma.

REACTIONS FROM TRANSFUSION OF PRESERVED BLOOD.

In this series of transfusions, 500 c.c. of blood were mixed with 650 c.c. of 5.4 per cent dextrose and 100 c.c. of 3.2 per cent dihydrin sodium citrate and stored at 3° to 5° C. All bloods were cross-matched with the recipient in addition to being grouped.

The period of storage is limited by haemolysis, and blood was regarded as unsafe when the degree of haemolysis was such that the recipient would develop haemoglobinuria. Dextrose citrate mixtures were used after periods of storage not exceeding 30 days. Heating of the blood before administration is unnecessary.

One thousand six hundred and four transfusions were given, the amounts varying from 50 c.c. of blood in infants to 500 c.c. of blood in adults. In 146 cases the blood was transfused within two hours of collection, and these fresh transfusions were taken as controls.

Chills and fever were the commonest reactions noted. These are usually ascribed to the presence of pyrogens, but in spite of all care to exclude pyrogens, the incidence of these symptoms was 3 per cent.

Urticarial reactions occurred in 1.4 per cent of cases. There was no connection between the allergic manifestations in donors.

Haemoglobinuria occurred in two cases after the use of blood after prolonged storage. Incompatibility of blood produced haemolysis and death in another case. There were two other cases for which there was no apparent cause. These may be explained by the transfusion of haemolysins active against the recipient's cells in unusually high titre, or storage may so damage corpuscles that they cannot withstand trauma in the capillaries of the recipient.

Jaundice was seen only once, in a baby, and was probably due to the underlying disease rather than to the transfusion.

There was one case of fatal cardiac embarrassment when a large transfusion was given rapidly to a child.

Reactions from stored blood do not vary from those seen after transfusion of fresh blood, but the incidence of haemoglobinuria depends on the preservative used and the period of storage. The two fatalities were due to accidental errors in technique.

CHEMOTHERAPY FOR GONOCOCCAL INFECTIONS IN WOMEN AND CHILDREN.

A hundred and four adult women suffering from gonorrhoea of all degrees

of acuteness were treated. After trial of various techniques, the most efficacious was found to be 2 grammes of M. & B. 693 daily for one week, commencing immediately the diagnosis is made. This was combined with local applications of 10 per cent protargol.

Nausea, headaches and skin rashes were the common toxic symptoms. Sodium bicarbonate usually relieved the nausea, but, in difficult cases, the dose of sulphapyridine may have to be reduced: 87.4 per cent were cured, i.e. swabs were always negative after the end of the first week of treatment. Four of the failures were due to inadequate dosage. Complications such as salpingitis were also quickly cured, and three cases of Bartholin's gland abscesses resolved without incision.

In gonococcal vulvo-vaginitis of children, the dose of sulphapyridine depends on the age and development of the child. The results were unsatisfactory, and only about half the cases were cured. Better results were obtained with two courses of chemotherapy separated by an interval of one and a half to two weeks.

Twenty cases of ophthalmia in children were all cured, a total dose of 3 grammes of sulphapyridine being sufficient. The children received irrigations as well, but all swabs became negative within a few days of commencing treatment.

The effect of sulphapyridine does not depend on the strain of gonococcus concerned but on the individual patients. Acute and chronic cases respond equally well. When rapid improvement does not take place, the chance of ultimate cure is poor. In children, regular administration of the drug, by night as well as by day, gives better results.

TREATMENT OF THE IMPACTED SHOULDER.

Evisceration is easy and safe, and should replace the difficult operation of decapitation in cases of impacted shoulder presentation. After traction on the arm, the chest wall is cut through with scissors and the thoracic viscera removed. The body of the child collapses and may then be delivered; only in difficult cases is removal of abdominal organs necessary.

General anaesthesia is not essential for this operation, and there is no intra-uterine manipulation with its risk of ruptured uterus. The difficulty of delivery of a decapitated head is also avoided.

T. N. A. Jeffcoate.

The Canadian Medical Association Journal

Vol. xlii, No. 5, May 1940.

*Mammary tumours produced in rats by the action of oestrone tablets. R. L. Noble, C. S. McEuen, and J. B. Collip.

*The treatment of placenta praevia. W. A. Scott.

*The treatment of puerperal sepsis. L. T. Armstrong.

Vol. xlii, No. 6, June 1940.

*The induction of labour. W. P. Tew.

*The management of delayed labour. G. C. Melhado.

*The recognition of late toxaemia of pregnancy in its incipiency. H. F. Dyer.

*Hysterosalpingography in the diagnosis of gynaecological affections. J. E. Gendreau and O. Dufresne.

Vol. xliii, No. 1, July 1940.

*Maternal mortality. W. G. Cosbie.

*Caesarean section. Nathan Shaul.

MAMMARY TUMOURS PRODUCED IN RATS BY THE ACTION OF OESTRONE TABLETS.

A special study has been made of the relation of the oestrogens to the production of mammary cancer in mice of certain strains with a susceptibility to cancer. Females which had raised litters showed a higher incidence to cancer than those which had not mated. This fact, when considered with the work of various investigators who found that the removal of the ovaries prevented the development of breast cancer, made it apparent that oestrogens are highly important causative factors. These same investigators found that the earlier in life that oöphorectomy was performed the smaller was the percentage of mice which subsequently developed cancer. Recently, Woolley, Feketi and Little noted, however, that even if female mice were deprived of ovaries within 24 hours of birth, yet 26.8 per cent of them eventually developed mammary growths. It was presumed that adrenal gland secretion may have replaced oestrogen.

Male mice of the strains highly susceptible to cancer do not spontaneously develop mammary cancer, but if these animals are treated with oestrogen, the mammary tissues show signs of stimulation and eventually malignant changes. More recent evidence has shown that oestrogen treatment may be followed by cancer of the mammary glands of rats of a species in which spontaneous cancer of the breast is very rare. Furthermore, benign fibro-adenoma has also been observed in these. It was also noted that there were changes suggestive of ovarian or pituitary malfunction in these animals. These fibro-adenomata when transplanted could not be induced by oestrogen treatment to undergo malignant change. McEuen made daily subcutaneous injections of oestrogen in a series of rats and gave oral feedings to another group. Of the injected series, two females developed histologically verified cancers after 530 to 624 days of treatment with 30 μ-grammes of oestrone. No tumours of the breast were found after feeding 1,500 international units of crude oestrogen for 700 days. Two other observers noted the occurrence of cancer in a spayed rat after long series of injections. These few results have stimulated further investigation.

In the experiments carried out by these authors an attempt was made

to induce mammary carcinoma in rats by the subcutaneous implantation of oestrone tablets. A study of the protective and curative action attributed to the thyreotrophic extracts of the anterior pituitary gland by Cramer and Horning was made, but the report will be given in a later communication.

The following methods of investigation were employed. Rats of the black hooded strain, maintained in the laboratory for the last eight years, were used in the experiments. They were fed only on purina fox chow. Crystalline oestrone in tablets of 1 to 7 mg. in weight were made by great pressure without any binding material. These tablets were implanted singly or in groups in the subcutaneous tissues of the back in female rats five to seven days old. The mammary glands were investigated regularly, and thickening or nodular formation of their substance was noted. Histological biopsy of the glands were made only when the masses were of 1 c.c. in diameter. A number of the rats also received daily subcutaneous injections of 0.05 c.c. to 0.25 c.c. of a special thyreotrophic substance from whole pituitary gland of the hog prepared by isoelectric precipitate as prescribed by Collip. This preparation contains 0.63 per cent of total solids. It had been shown that injections of 0.04 c.c. twice daily for five days into guinea-pigs of 200 gr. had resulted in enlargement of the thyroid gland up to an average of 69 mg. of weight. The results of these investigations are given in two short tables. It appears that the total dosage did not appreciably affect the time at which tumours first appeared. The first tumour was palpable after 226 days of treatment. The tumours were slow growing and were not near the site of implantation of the tablet or tablets. Following this method of treatment, tumours were found in the mammary glands of 28 out of 49 rats. When the glands were examined histologically, there were signs of general stimulation, the glandular tissue was increased in amount, the ducts showed increase in the number of cells and were distended with secretion, in some cases forming cystic masses. The tumours showed extreme cellular hyperplasia, but no rupture of the basement membranes or invasion of the stroma. Other effects were a retardation of bodily growth, enlargement of the pituitary gland with adenoma formation, ovarian atrophy, uterine fibrosis with squamous-cell metaplasia, dilatation of ureters and renal pelves, the formation of vesical stones, the occurrence of ovarian abscesses, and the occurrence of lympho-sarcoma in rats which had a spontaneous tendency to the development of this growth.

Two tables of results and three detailed microphotographs are included and a very full bibliography is appended.

The Treatment of Placenta Praevia.

Antenatal haemorrhage is an outstanding cause of maternal mortality, and has third place, being exceeded only by puerperal sepsis and the toxaemias of pregnancy. Placenta praevia as a cause of death is about equal to other forms of haemorrhage. At present there is no routine method of treatment, and, if there were, Caesarean section would probably give the

best results for mother and child. It is the author's opinion, however, that it is safer not to be fixed by routine, but to choose methods suitable to each individual case. One disadvantage of the routine employment of Caesarean section is that, through failure to make vaginal investigation, a clear diagnosis is not established, and needless operations are performed with increased dangers for future pregnancies. In the first place, all cases of placenta praevia should, when possible, be treated in hospital, yet the nature of these cases is such that it is inevitable that emergencies will arise when hospital care is unavailable. Many of these severe cases, however, might have had the benefit of hospital advantages had premonitory symptoms been duly noted and their warnings appreciated. Bleeding in any degree during the last half and especially the last few weeks of pregnancy is an important danger signal never to be neglected. In the author's series two patients refused to enter hospital and two others already in hospital refused to remain, simply because the premonitory haemorrhage was slight.

The author presents two short tables. In the first there were 81 cases of placenta praevia, 44 having profuse original haemorrhage, while 37, 45.6 per cent, had slight premonitory haemorrhage. Of these latter cases 6 had subsequent severe haemorrhage, 3 requiring transfusion, while in 7 cases there was complete placenta praevia. Of the 37 cases with slight premonitory bleeding, 11 were delivered spontaneously, 11 with hydrostatic bag, 8 by Caesarean section, 4 by version, 2 with low forceps, and 1 treated by vaginal packing died within 20 minutes of admission. In this series there was 1 maternal death, 26 babies were born alive, of which 7 died within 12 days, and of these 7, 4 were maldeveloped. There were 11 babies dead at birth, 6 being monsters.

In considering treatment, the most important factor is the presence or otherwise of a complete placenta praevia, the amount of the placenta covering the cervix varying, of course, with the dilatation of the cervix.

In another table the author classifies the cases into complete and incomplete placenta praevia. There were 81 cases, of which 7 were complete and 64 incomplete. In the latter 64, the placenta was palpable in 44 and not palpable in 20. In deciding on treatment, the factors which will influence the method are the situation of the placenta, the amount of haemorrhage, the parity of the patient, primipara or multipara, condition of labour, whether in progress or not, how it is progressing, the duration of the pregnancy, the presentation of the baby, and the condition of the child, whether alive or dead.

In a table the author gives his method of treatment in 81 cases. The methods of treatment and results were: spontaneous delivery in 28 cases, 6 dead babies; hydrostatic bag, 15 cases, 7 dead babies; classical Caesarean section, 11 cases, 4 dead babies; lower segment Caesarean section, 3 cases, no deaths; rupture of the membranes, 11 cases, no deaths; version, 9 cases, 6 deaths; delivery by the forceps, 3 cases, 1 death.

An analysis is given of 17 cases of complete placenta praevia. Caesarean

section was performed in 9 cases, 7 classical with 3 dead babies, 2 lower segment with no dead babies; hydrostatic bag, 3 cases with 2 dead babies, version, 2 cases with 2 dead babies; spontaneous delivery, 2 cases with 2 dead babies. Thus of a total of 17 cases, there were 10 dead babies. Cases of incomplete placenta praevia were also reported, 64, with 15 dead babies. In the total series of 81 cases there were 2 maternal deaths, a mortality of 2.4 per cent, 1 dying undelivered and the other dying of pulmonary embolism on the twenty-third day post-partum, having developed phlebitis on the seventeenth day. These results compare very favourably with reports from other clinics. It is the author's opinion that vaginal packing greatly increases the risk for all other forms of treatment. It is only of value when haemorrhage is severe and long transport to hospital is necessary. In cases of version, the foetal death-rate was high, but the babies were premature, and two of the patients were suffering from toxaemia of pregnancy.

THE TREATMENT OF PUERPERAL SEPSIS.

Infection and haemorrhage are the two outstanding dangers which imperil obstetric and surgical cases, and frequently they occur together. This is especially applicable in obstetrics. The prophylaxis of sepsis, therefore, entails the avoidance of haemorrhage and the treatment of anaemia. This latter condition, as well as the patient's general health, should receive attention by the employment of suitable medication, together with a properly balanced diet, the addition when necessary of synthetic vitamins, and due attention to rest. Antenatal care should anticipate dangers and difficulties, such as malpresentations and toxaemias. The employment of Caesarean section must be judicious and the indications must be defined on the soundest obstetric principles. Many unnecessary operations have been performed, often by those unqualified for such undertakings. The application of the forceps and the utilization of episiotomy are not to be urged, but when well chosen have many advantages. Strict antiseptic attention to the vulva, the surgeon's and attendants' hands and instruments must be given. Many useful antiseptics are available; amongst them dettol has a high place. In recent years it has been shown that the most serious puerperal infections are air-borne and are sprayed as droplet infections from the respiratory passages of attendants, the patient, or by visitors. Suitable masks should be worn by all during labour.

The streptococcal group of bacteria is the most dangerous of all these. The haemolytic variety of the Lancefield group A is the chief offender; it is usually distributed by spray or droplet transference. It is most virulent, and causes the most serious infections. After this in order of frequency come haemolytic streptococci groups B, C and G, which are mild in their virulence; then anaerobic streptococci, bacillus coli, staphylococci, and bacillus Welchii and pneumococci. Fortunately against haemolytic streptococci there is an almost specific remedy in sulphanilamide. To employ this safely and to its greatest advantage, repeated bile and chemical tests are neces-

sary to show that it is carried in the blood-stream in the proportion of 8 to 14 mg. per 100 c.c. The dosage to maintain this concentration is extremely variable, and may range from 45 to 180 grains every 24 hours. The administration of the drug must be continued after the temperature has returned to normal and blood-cultures have become negative, unless the toxic effects of the drug demand reduced administration. Toxic manifestations include malaise, nausea, and vomiting, tinnitus and a moderate degree of cyanosis. Haematuria and oliguria demand reduction in the dosage. If there is a secondary rise in fever, or rash, or blood changes such as reduction in haemoglobin or blood-cells, the drug must be withdrawn. The appearance of agranulocytosis has occurred and is a serious condition. Sodium bicarbonate is the only other drug which may be used during treatment with sulphanilamide.

Should the temperature during the puerperium reach 100° F. or more on two consecutive days, puerperal sepsis must be suspected. Bacteriological investigation of the upper vagina, the urine and blood-stream must be made and cultures of these both anaerobically and aerobically must be instituted. The patient must be strictly isolated and segregated. She must be nursed in a comfortable airy room, and a generous diet and sufficiency of fluids supplied. Fowler's position must be employed to limit infection to the pelvic region. The total fluid intake and output should be calculated daily. When the patient is acutely ill, intravenous medication with 10 per cent glucose with saline, or saline by itself, may be given, or the saline may be substituted by distilled water and when the haemoglobin and blood-plasma protein are low, blood-transfusion is indicated. It is important to follow throughout the course of treatment the blood chemistry of patients who are ill. General peritonitis is treated by intravenous therapy together with the use of an indwelling duodenal tube, together with continuous or intermittent suction; morphia must be administered and the electric cradle employed. When paresis of the bowel is present, decompression of gastro-intestinal contents may be effected with the Miller-Abbot tube, and attempts to obtain bowel movements should be avoided. Laxatives and pituitrin are contra-indicated as they extend the peritoneal infection. Should diarrhoea develop, it must be controlled with opiates. Paregoric in doses of 2 grains every two hours for four doses should be given.

Local treatment, such as intra-uterine douching, is harmful, though intra-uterine instillations of glycerine are useful. Uterine exploration and curettage are dangerous and liable to promote greater spread of the infection. Vaccine therapy and antistreptococcal serum appear to have little benefit. Surgical measures such as hysterectomy and the ligation of veins are condemned. Drainage of the pelvis and of any local infection may, however, be permissible.

Induction of Labour.

The induction of labour means the interruption of pregnancy at or near term, and in the present paper it is confined to the termination of preg-

nancy after the child has become viable. Louise Bourgeoise, in 1608, midwife to Marie de Medici, was one of the first to introduce it as a therapeutic measure. Smellie employed the procedure in 1756, and Denman, in 1793, reported induction in 20 cases of contracted pelvis. Induction has since then been employed very successfully, but the indications are not at present well defined.

The indications are contracted pelvis, diseases incidental or accidental to pregnancy, habitual death of the foetus after viability, post-maturity, and overgrowth of the child.

Contracted pelvis. Avicenna, A.D. 979 to 1037, appears to have been the first to employ induction for contracted pelvis. In the nineteenth century the practice was very common, because Caesarean section was followed by such a high mortality. In cases of major pelvic contraction, Caesarean section at or near term is the proper treatment. In moderate degrees of contraction it is a safe procedure to let the patient have a trial of labour, as frequently this is successful and, if the patient is under observation in suitable surroundings, Caesarean section can be undertaken if necessary.

Diseases incidental to pregnancy are pre-eclampsia and eclampsia, placenta praevia, accidental haemorrhage, and polyhydramnios. In the management of these conditions it is essential to terminate pregnancy before the mother's or baby's life is too greatly endangered. Pre-eclampsia will frequently respond well to treatment, but if it increases in severity despite this, if blood-pressure is rising, albuminuria increasing, the output of urine is diminishing, headache has appeared, ocular symptoms or retinal symptoms have appeared, then induction is clearly indicated. The method of induction will depend on the urgency of the case. When there is some degree of disproportion, if the head is above the pelvis, Caesarean section is the method of choice; but if the patient is a primigravida, with the head well within the brim, the membranes should be ruptured, liquor permitted to escape, and 0.5 c.c. of pituitrin administered. If there is a poor response, a bag or bougie must be used. The chief rules for dealing with a case of toxaemia are to attempt to bring the patient as near as possible to term, at the same time avoiding too long delay and by terminating pregnancy by the methods most suitable to the case.

Eclampsia is treated first by gaining adequate control of the convulsions at the earliest possible moment, by reducing oedema and assisting delivery. If labour starts it may be permitted to proceed. When labour pains are absent, the membranes may be ruptured.

Placenta praevia is usually best treated by Caesarean section, but in suitable cases rupture of the membranes alone, or rupture of the membranes with the application of Willett's forceps, or the introduction of a hydrostatic bag may be employed. Haemorrhage is usually treated by rupturing the membranes and occasionally by packing the vagina and cervix in addition. Very occasionally Caesarean section is necessary. Polyhydramnios is usually treated by rupture of the membranes. Chronic nephritis with failing renal function should be treated by termination of pregnancy

by medicinal induction or one of the mechanical methods. Pulmonary tuberculosis does not appear to be benefited by the induction of labour. Cardiac disease also does not appear to be benefited by induction; if a difficult labour is anticipated, Caesarean section is the better treatment. Diabetes, when strictly treated, seldom presents difficulties, but should these measures fail induction under spinal anaesthesia may be necessary. Psychosis does not of itself demand induction. Habitual death of the foetus after viability presents serious problems, but induction by one of the methods should be tried. Post-maturity and possible overgrowth of the child may cause difficulties during labour. A good general rule is to allow the patient to go a week beyond her expected time and then mechanical methods should be instituted. The methods of inducing labour are reviewed.

Medicinal induction. Ten thousand units of oestroform are given orally in the morning and a copious enema an hour later; another hour later 10 grains of quinine hydrochloride are given. A quarter to 1 c.c. of pituitrin is given every half to one hour for 6 to 8 doses. This may be administered by saturating 1 c.c. of pituitrin in a nasal plug, which is inserted hourly six or eight times. Quinine is now believed to cause foetal deaths.

Mechanical methods. Puncture of the bag of waters is effectual in 98 per cent of cases. It is most effectual when the head is low in the pelvis, the cervix soft and less than one inch in length and the patient is near term. Induction by means of bougies is effectual in about 75 per cent of cases and is more dangerous than the two previous methods. The use of a hydrostatic bag is usually limited to certain cases of placenta praevia.

A short bibliography is appended.

THE MANAGEMENT OF DELAYED LABOUR.

The average duration of labour in primipara is 12 to 18 hours, but may last considerably longer without any bad effect on child or mother. The causes of delay are often complex; they may be due to weak expulsive forces, mechanical faults, or combinations of these; they may occur during the first or second stages. Primary inertia is a common cause of delay, especially in certain types of patients. Poor uterine contractions are often associated with great pain. It was formerly taught that the conservation of liquor amnii to act as a cervical dilator was important, but the effect of rupturing the membranes does not appear to be in any way harmful. It has been claimed that dilatation of the cervix is chiefly effected by the arrangement of the uterine muscle, the longitudinal and oblique fibres of which exert contractions in such a manner as to dilate the cervix and lower uterine segment by their action over the presenting part. It is often noted that malpresentations, such as occipito-posterior, are associated with primary inertia and this appears to be due to the unfavourable mechanical application of the presenting part.

There appear to be three factors causing uterine inertia, (1) incoordination of the uterine muscular action, (2) endocrine, and (3) chemical deficiency. Irregular muscular action is frequently expressed in the

development of a contraction ring in the lower uterine segment, and this is often seen in combination with malpresentation, such as a persistent occipito-posterior position, and poor uterine contractions. Absence of oestrogenic substances is doubtless an important cause of primary inertia, as Jeffcoate has shown that administration of these substances is successful in 56.8 per cent of these cases. Diminution of calcium in the blood below a certain level is often associated with inertia and poor response to the administration of oxytocic substances.

A fairly full bibliography is appended.

THE RECOGNITION OF LATE TOXAEMIA OF PREGNANCY IN ITS INCIPIENCY.

Probably 10 per cent of pregnant women show signs of toxaemia and about a third of all maternal deaths are due to late toxaemia. It has been estimated that 50 per cent of women who have suffered from toxaemia show signs of chronic arterial disease or chronic nephritis when examined 5 years later. The condition may be divided into pre-eclampsia and eclampsia, but the difference is merely one of degree, rather than of kind. There are four main signs: (1) hypertension, (2) albuminuria, (3) oedema and (4) convulsions. It is highly probable that when the first three of these signs are present, the toxaemia is well established. In the majority of cases the condition progresses in spite of treatment.

Four years ago the author undertook to determine whether or not there were earlier signs of toxaemia. He acted on the assumption that vascular damage is the basis of pathological changes in the liver, kidneys, brain and heart and that the eclamptic toxin produces a spasm of the arterioles, which, continued over a time, produces changes in these organs, and further that the amount of urine excreted during the night exceeds the amount of that excreted during the day. This latter sign, together with changes in the retinal vessels, gives an early warning of the incipience of toxaemia. He therefore carefully calculated and measured the amount of urine passed between 8 a.m. and 8 p.m. and that passed between 8 p.m. and 8 a.m. These two amounts were kept separate, measured and compared and he concluded that patients in whom the daily output of urine exceeded the nocturnal output were in no danger of developing toxaemia, and conversely when the nightly output exceeded the daily, the patients were in danger of developing toxaemia; in this latter group a period of 6 to 8 weeks elapsed before the recognized signs of toxaemia appeared. He furthermore found that when patients with this earlier warning of toxaemia were treated with large doses of vitamin C, the daily output of urine again became dominant and the danger of developing toxaemia appeared to be eliminated. The author cited 250 consecutive cases, 5 of which showed this increase of nocturnal urine to be in excess of that passed during the day. They were treated with large doses of vitamin C and no further development of toxaemia ensued.

A short case routine is given.

HYSTEROSALPINGOGRAPHY IN THE DIAGNOSIS OF GYNAECOLOGICAL AFFECTIONS.

Hysterosalpingography was first attempted in 1914 and is now widely used. The method is simple and harmless and when radiological diagnosis of diseases of the uterine cavity and Fallopian tubes is made with lipiodol or skiodan acacia, much information is supplied. The only contra-indications are acute infection, abundant haemorrhage or pregnancy. The radiological appearances of the normal uterus show a triangular shadow with base upwards and apex pointing downwards and with a slightly curvilineal outline. The tube canals filled with opaque material give filiform shadows starting at the superior angles of the uterus, curving downwards and outwards, slightly enlarging and becoming continuous with intra-peritoneal deposits of the opaque substance. When there is chronic infection of the tubes which alters the muscular walls, the radiological appearances are those of a wide festooned outline of dark thin shadows ending in a broad dark shadow. Acute infections which alter the mucosa partially or completely, cause obstruction of the tubal lumina. Tumours outside the uterine cavity alter the shape but not the size of the shadow of the cavity, whereas tumours of the wall of the uterus increase as well as distort the shadows of the body. Intra-uterine tumours cause irregular outlines of the shadows, which are different with every kind of tumour. The indications for hysterosalpingography are : (1) uterine haemorrhages, the causes of which are not revealed by ordinary gynaecological examination, (2) sterility, to discover its origin and locate the situation of the obstructing lesion, (3) genital pains (with no apparent cause), to determine their aetiology, (4) pelvic tumours, to determine their differential diagnosis.

In cases of metrorrhagia, hysterosalpingography will reveal the presence of a polypus, retained placenta, uterine tumour or the exact spot where a carcinoma is beginning to grow and will greatly assist in the subsequent curettage when this is necessary. Occasionally genital pain may be a troublesome symptom, the cause of which cannot be determined by general or local exploration. Hysterosalpingography may reveal the existence of a clinically inconspicuous spasm, a congenital malformation, an inflammatory lesion or a neoplastic formation in the uterus.

Pelvic tumours may present some difficulties in differential diagnosis. Hysterosalpingography will readily assist in making a differentiation between a fibromyoma and cyst of either inflammatory or neoplastic origin.

MATERNAL MORTALITY.

The average maternal death-rate for Canada for 12 years ending in 1937 was 5.3 per 1,000 live births, or 1,230 women died annually from the results of pregnancy. These results compare unfavourably with those of other countries.

The chief causes of death are puerperal sepsis, toxaemias of pregnancy

and puerperal haemorrhage. Unfortunately the death-rate due to abortion is included in the statistics and it seems unfair that these, together with deaths from ectopic pregnancies, should be included in the census of maternal deaths due to pregnancy. It is conservatively estimated that two-thirds of the deaths from abortion are due to criminal interference. Among 1,710 cases admitted with abortion, 40 women died, whereas in a 10-year period only 60 women died in the obstetric department.

Puerperal sepsis is the chief cause of maternal deaths, being responsible for more than one-third of these; it is the great disappointment of obstetrical practice that the introduction of antiseptics has not produced the great results that it has in surgery. The outstanding reason for the great occurrence of sepsis appears to be failure to recognize the source of infection, failure to observe strict antiseptic technique and excessive manipulations and interferences.

Colebrook and his colleagues have shown that the haemolytic streptococcus is responsible for the great majority of fatal cases. It is the same type which causes scarlet fever, tonsillitis, erysipelas, impetigo and other localized infections. Many so-called influenzal or common cold illnesses are due to, or associated with, this organism and about 7 per cent of normal healthy persons are carriers of this microbe in their nasal pharynges, while about 3 per cent harbour it in their skins. Colebrook has shown that haemolytic streptococcal puerperal infections usually arise from an infection in the nasal pharynx of the doctor, nurse or other attendant of the patient. He further showed that the organism is air-borne and that cultures taken from the air in the vicinity of heavily infected patients were invariably positive and it can be seen how widely and effectively infection may be transported through the air. The second type of puerperal infection with anaerobic streptococci, colon bacilli or staphylococci is sometimes the result of bad craftsmanship. This intervention type of infection is nearly twice as high in Canada as in Holland, where training in midwifery is advanced, antenatal supervision extensive, where the tendency to send abnormal cases to hospital is widespread and where degrees of pelvic deformity are rare.

Prevention of puerperal sepsis is an involved problem. It is an obvious dictum that no patient should be confined in a home where streptococcal infection is known to exist. Doctors and nurses should be free from infection and the greatest care must be taken to effect sufficient sterilization when they have been in attendance on infected patients. All attendants should wear efficient masks and the whole routine of surgical cleanliness and asepsis should be followed. Vaginal examination should if possible be replaced by rectal examination. In all good hospitals a labour room should be provided wherein the technique should be as rigid as that observed in the operating room. The wearing of masks, gowns and gloves by doctors and nurses can here be followed and this may also obtain in private homes. In overcoming unavoidable breaks in technique, dettol cream has been suggested for sterilizing the vulva and perineum, or the

hands of medical and nursing attendants. Colebrook is of the opinion that this practice has reduced the infection rate by 50 per cent. When infection has occurred, immediate bacteriological examination should be made and the patient and her nurse isolated.

At present much is heard of the efficacy of sulphanilamide treatment, but it may well be that the virulence of the special organism varies in a cyclic manner. A table is introduced to illustrate this point. From 1922 to 1926, out of 2,231 deliveries the septic death-rate was 5.4 per 1,000, while during 1927 to 1938, out of 9,729 the septic death-rate was 1.2 per 1,000. There was a definite decline in fatal cases between the epidemic in 1924 and the introduction of sulphanilamide in 1936.

There is an increasing tendency for patients to be confined in hospital instead of at home and by comparing statistics of Quebec, where less than 16 per cent enter hospital, and British Columbia, where about 80 per cent do so, it appears that perhaps the death-rate is less among those confined in hospital. As regards women resident in the city and those coming in from outside to the same hospital, the death-rate is about twice as high among the non-residents.

Toxaemias of pregnancy are to be combated by efficient antenatal care. Difficulties, however, arise because many women do not avail themselves of this care, and much propaganda for the education of the public is necessary. As regards eclampsia, a sound dictum is to treat the eclampsia and leave labour to run its own course. Caesarean section has no place in its treatment to-day.

Haemorrhage is a most tragic cause of maternal death and one feels that such should, in almost every case, be prevented. Hospital treatment, blood-transfusion and Caesarean section for all major degrees of placenta praevia, have done a great deal to lower the maternal death-rate from this condition. Accidental haemorrhage is treated by combating shock and haemorrhage, and delivery is usually effected on conservative lines, with the exception of severe types of concealed haemorrhage with damaged or inactive uterine wall. Post-partum haemorrhage appears to be associated with shock and collapse and can often be prevented by proper conduct of labour, wherein exhaustion of the mother is avoided, when anaesthesia is used and when delivery is effected with a minimum of trauma. It is good practice to maintain uterine tone, possibly with oxytocics after the birth of the child, and to avoid too hasty attempts at delivering the placenta. Severe haemorrhage produces severe anaemia and is best treated by blood-transfusion.

Caesarean section improperly used is an outstanding cause of maternal mortality. It is not, however, the cause of all deaths which follow its use, but rather the conditions which call for its performance. The chief cause of death following the operation is peritonitis and this again is attributed to an ill-chosen time for the operation. It is notable from statistics that the operation is almost three times as frequent in private as in hospital patients. The incidence of its performance has undoubtedly decreased in the last decade. The employment of the low segment as

compared with the classical operation has done much to widen the usefulness of this measure and reduce its associated fatalities.

It remains, however, to point out that skilful obstetricians are urgently needed and training in this art, both for physicians and nurses, requires greater amplification, and while the greater and more thorough training of the professions is demanded, the education of the public is also a crying need.

Many useful tables are given in the text and a full bibliography is appended.

CAESAREAN SECTION.

In approximately 7 years between 1932 and 1939, the author delivered 1,449 cases. There was no maternal death-rate and the foetal death-rate was 2.8 per cent. There were 26 Caesarean sections, of which only 2 were classical, 24 being low cervical double-flap operations, an incidence of 1.9 per cent. There were no maternal deaths, but a morbidity of 11 per cent. Two infants died, one just before the operation was started and the other 14 days afterwards. The indications for the operation were disproportion in 9 cases, central placenta praevia 2, old primigravida 1, previous Caesarean section 1, previous still-births with difficult deliveries 3, prolonged sterility 3, and single cases were performed for cardiac disease, large breech and bilateral nephrolithiasis. Spinal anaesthesia was employed in 24 cases, ether in 1 and gas and oxygen in 1. Spinal anaesthesia was the most satisfactory in these cases. No ill effects have been seen by the author from its employment, though many authors do not recommend it and some oppose it. Palliez and Gernez report 131 consecutive Caesarean sections without any deaths, spinal anaesthesia being employed in 101 cases. These authors are of the opinion that their good results were due to this form of anaesthesia. Cosgrove has employed spinal anaesthesia very extensively and has had only one death which could scarcely be attributed to the anaesthetic.

Caesarean section may be classified as elective or imperative. For the elective type, the mortality rate should always be low. In the imperative group are included neglected dystocias, patients exsanguinated from placenta praevia or detached placenta and toxaemic patients. The author agrees with Schumann that when disproportion is definitely present, even though not insuperable, the case should be treated by Caesarean section, preferably without a test of labour, as this greatly favours the outlook for the life of the child and the well-being of the mother. Caesarean section is vastly preferable and a much better procedure than a difficult forceps delivery or version, with great risks of foetal intracranial haemorrhage or Erb's paralysis, not to mention extensive damage to the maternal pelvic fascia and sacro-iliac articulations.

The author quotes Schumann, who reports a summary of 120 consecutive elective Caesarean sections. There were no maternal deaths, a morbidity of 6 per cent and an infant mortality of 2.5 per cent.

It is a highly beneficial measure to have intravenous injection continued during the operation, and in cases in which haemorrhage has previously been severe blood-transfusion should be carried out before and during the operation.

A short bibliography is appended.

J. LYLE CAMERON.

The Medical Journal of Australia

June 8th, 1940.

*Vitamin K.

June 15th, 1940.

Chorea gravis in pregnancy. H. Patterson.

Uterine hypoplasia treated with follicular ovarian hormone. T. H. Small.

*Abnormal attachment of the foetus to the placenta. J. S. Green.

June 22nd, 1940.

*Rapidly growing fibrosarcoma of the uterus. H. J. Ham.

June 29th, 1940.

Cryptophthalmos or ablepharia: a survey of the condition with a review of the literature and the presentation of a case. I. Brodsky and G. Waddy.

VITAMIN K.

Under the heading of "Current Comment" a short account is given of the present knowledge of the characteristics of vitamin K.

This vitamin is fat-soluble and is present in large amounts in certain green vegetables, particularly in lucerne and spinach. The existence of such a vitamin was first suspected by Dam of Copenhagen in experiments in lipoid metabolism with newly hatched chicks which were kept on a fat-free diet and thereafter developed a tendency to haemorrhage. Further research showed that a new fat-soluble vitamin was essential for the prevention of haemorrhage. The initial K was derived from the Dutch word Koagulation.

Further research by Dam and his colleagues showed that vitamin K deficiency led to a lowered blood prothrombin level and that when this is below one-third of normal spontaneous haemorrhage occurs. Sufferers from vitamin K deficiency behave in many ways like haemophiliacs.

Vitamin K can be produced by bacterial action in the lower intestine and can be absorbed from thence even when the diet is vitamin-free. As a result animals and man rarely show signs of vitamin K deficiency unless there is a defect of absorption.

Absorption of fats from the bowel is largely dependent upon the action of bile. When there is a biliary deficiency, as in obstructive jaundice, biliary fistula and hepatic degeneration, the prevention of the absorption of fat-

soluble vitamin K will lead to a lowering of the level of prothrombin followed by a tendency to haemorrhage. The treatment consists essentially in feeding with bile or bile salts together with large amounts of vitamin K to supplement the natural supply.

Vitamin K deficiency would explain the occurrence of haemorrhagic disease of the new-born. A full-time infant has usually one-sixth to one-third of the adult proportion of prothrombin and premature infants have much less. In the more deficient infants the condition manifests itself in a haemorrhagic state. A low prothrombin level in the infant can be raised by feeding the mother with vitamin K before delivery or the infant directly after birth. Infants with icterus gravis or anaemia neonatorum which have a tendency to haemorrhage, may be relieved of this tendency by feeding with vitamin K.

Abnormal Attachment of the Foetus to the Placenta.

J. S. Green of Melbourne shortly describes two cases of unusual attachment of the foetus to the placenta.

In the first case the patient, a second para, was in labour of a premature infant which was presenting by the feet. There was some difficulty in delivery and ultimately the hand was introduced into the amniotic sac. Attached to the front of the foetus was a sac containing loops of bowel and this sac was furthermore closely applied to the placenta. It was found impossible to extract the foetus until the placenta was manually removed at the same time. Inspection after delivery showed that the ventral wall of the foetus was formed mainly by the thin wall of the sac and the placenta.

The second patient, pregnant for the sixth time, was treated as an emergency for severe bleeding from a placenta praevia. The foetus was delivered by Caesarean section and found to be a monster. The foetus was in an attitude of extension. The ventral and caudal aspects of the foetus were replaced by the placenta. An anus was present but the external genital region appeared to have merged with the lower end of the placenta.

Two excellent diagrams of the foetal abnormalities are given with the description of these cases.

Rapidly growing Fibrosarcoma of the Uterus treated by Deep X-ray Therapy.

H. J. Ham describes the case of a patient transferred to his care at Prince Henry Hospital, Sydney, for treatment of advanced fibrosarcoma of the uterus by deep X-rays.

The patient was a Czech aged 30 years who was first seen by Dr. F. Brown Craig four months before her transfer; when the case was diagnosed as one of myoma of the uterus. At that time she had a baby aged 4 months which she was nursing at the breast. For this reason she was advised to wait until she had weaned the baby before submitting herself to operation.

At the operation three months later the uterus was found to be enlarged to the size of a 20 weeks' pregnancy and the condition was diagnosed as such after a 2-inch incision had been made into the uterus down to what was taken to be decidua. A cyst was removed from the right ovary and the abdomen closed. Aschheim's and Zondek's test was found to be definitely negative.

Three weeks later the abdomen was again opened and a rapidly growing neoplasm was found extending from the uterus to the abdominal wall. Removal of the tumour was impossible and within two weeks from this second operation the tumour had forced apart the edges of the incision and was growing like a large mushroom on the surface. A biopsy was carried out and the report was given that while histologically the growth was a fibromyoma with many areas of rapid growth it must be looked upon as malignant.

Treatment with deep X-rays was carried out over a period of three months with recession of the abdominal tumour and disappearance of the mass outside the abdominal wall. A year after the end of treatment the patient was in good health with a well-healed abdominal scar.

R. H. B. ADAMSON.

The Journal of the American Medical Association

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*Prostigmine methylsulphate for delayed menstruation. S. Soskin, H. Wachtel, and O. Hechter.

Vol. cxiv, No. 22, June 1st, 1940.

*The treatment of habitual abortion with vitamin E. Report of the Council on Pharmacy and Chemistry.

Vol. cxiv, No. 23, June 8th, 1940.

*Acute inversion of the puerperal uterus. W. Harer and J. Sharkey.

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*Symmetrical cortical necrosis of the kidneys. C. Davis.

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*The treatment of prepubertial vulvo-vaginitis with a new synthetic oestrogen. J. Russ and C. Collins.

Vol. cxiv, No. 26, June 29th, 1940.

*The treatment of nephrotic oedema. A. Goudsmit and M. Binger.

*The use of desoxycorticosterone acetate therapy in Addison's disease. E. McCullagh and E. Ryan.

ANOREXIA NERVOSA OR HYPOPITUITARISM?

The authors describe three cases of the syndrome variously called anorexia nervosa, hypopituitarism or incipient Simmonds's disease, and discuss the literature on the disease.

There is great difficulty in deciding whether to put these cases down to pituitary hypofunction or whether to invoke a psychical cause. In many cases, with the solution of various personality problems, the appetite returns and the endocrine features vanish—a fact that leaves doubt as to their primary aetiology.

There is no regularly satisfactory treatment. Some patients recover seemingly spontaneously, as did one of the authors' patients. Two of the patients seemed to improve after insulin therapy, although one of them after a relapse did not respond so strikingly to insulin on a second trial.

The criteria for cure have not been established. In one case, after apparently complete recovery from both clinical and laboratory standpoints for a period of four years, amenorrhoea and then oedema developed without preceding significant loss of weight and following comparatively slight emotional trauma. It appears that some underlying disturbance, somatic, psychic or psychosomatic, may persist even when a patient seems to have fully recovered.

It is possible that the clinical picture of anorexia nervosa develops somewhat as follows: certain individuals may react to emotional conflict by developing anorexia. As a result, then, of a diminution of the normal stimulus to appetite which regular food intake produces, this anorexia may become prolonged and self-perpetuating. With the consequent loss of weight all of the unusual features associated with the cases described may appear purely as a physiological response to weight reduction and semi-starvation. Why only few individuals will react to emotional conflicts in this manner, while most do not, can be explained only if certain necessary conditioning factors are assumed. Here perhaps lie the so-called primary endocrine factors. The management of anorexia nervosa is often most satisfactory when directed largely through psychic channels.

RENAL LESIONS FOLLOWING THE ADMINISTRATION OF HYPERTONIC SOLUTIONS OF SUCROSE.

The authors review the experimental work of Helmholz in 1933 on the effect on the kidneys of rabbits of the injection of hypertonic solutions of sucrose, and that of Lindberg, Wald and Barker in 1939 on dogs. The authors then describe 6 cases in man and conclude that in view of the uncertainty of recovery from cloudy and granular degeneration of the cells of the convoluted tubules, it seems inadvisable to inject hypertonic solutions of sucrose into people with any renal lesions. In any case repetition of the dose should be avoided except at intervals of several weeks.

THE TREATMENT OF DELAYED MENSTRUATION WITH PROSTIGMINE.

The important role of hyperaemia in the oestrous phenomenon in rats

suggested that delayed menstruation might be due to lack of vascular response rather than to endocrine malfunction.

On the basis of the physiological mechanism of oestrous hyperaemia, 25 women suffering from delayed menstruation were treated with prostigmine. Menstrual flow invariably resulted, usually in 30 hours, never later than 72 hours after the injection.

Prostigmine has no effect on early or prolonged amenorrhoea due to endocrine malfunction or to local organic changes, and the constancy of the results in menstrual delay and the lack of effect on pregnancy make it possible to use prostigmine as a combined treatment for menstrual delay and a therapeutic test for pregnancy.

THE TREATMENT OF HABITUAL ABORTION WITH VITAMIN E.

The first half of this paper consists of an examination of Malpas's analysis of abortion sequences. The main difference between his theory and the modification advanced by the authors is that he considers the likelihood of a further abortion becomes constant after three successive abortions whereas they consider it decreases indefinitely. Their reason for modifying the theory is that they consider he did not take into account the fact that the expectation of pregnancy decreases with successive pregnancies.

They make the following conclusions: (1) The diagnosis of habitual abortion is not justified until the woman has had at least two consecutive abortions. (2) There is a marked tendency to spontaneous cure of repeated abortion. For example, if a woman has had two consecutive abortions the chances are about 1 to 3 that she will not have another.

The second half of the paper examines the clinical reports of vitamin E therapy. The authors summarise reports of the results obtained in the treatment of 175 cases of repeated abortion; 75 per cent of successful results were obtained. In the authors' opinion, many of the reports were vitiated by absence of evidence that all the abortions were spontaneous, and also in many instances the cases were not observed at the time of the previous abortion. They reach the following conclusions:

Claims that vitamin E is of value in the treatment of menstrual disorders, failure of lactation and vaginal pruritus cannot be accepted because of lack of sufficient clinical evidence.

The claim that vitamin E is of value in the prevention of habitual abortion cannot be accepted because of the lack of convincing clinical evidence. The diagnosis of habitual abortion in many of the published reports is open to question; the great variation in dosage of vitamin E and the lack of evidence that the preparations used were active make it difficult to attribute any effects claimed for it to the vitamin. Moreover, the expectancy of spontaneous cure in cases of so-called habitual abortion has not been accurately established.

The published results of the treatment of habitual abortion with vitamin E are sufficiently encouraging to justify further clinical experiment. Such

experiments are justified only if preparations of vitamin E of known activity are used and if adequate diagnosis and clinical control can be established.

ACUTE INVERSION OF THE PUERPERAL UTERUS. A RECORD OF 21 CASES.

In 8 years in Philadelphia the authors collected records of 15 cases of acute inversion of the uterus, a proportion of 1 case in 16,240 deliveries. The paper is based on these and further 6 cases. Suprafundal pressure was the cause in 9 cases, manual removal of the placenta in 5 cases and traction on the cord in 2 cases, giving an avoidable cause in 16 cases or 76 per cent. In one case an unduly short cord was responsible and in the remaining 4 cases no cause could be discerned.

In about half the cases the inversion occurred before the placenta was separated. Nine of the women died, a mortality of 43 per cent.

Prophylaxis must fundamentally be the proper teaching of the management of the third stage of labour in medical schools. The authors discuss the relative advantages of immediate and delayed replacement of the inversion. The divergence of views they ascribe to the fact that no one obstetrician can have comprehensive experience of the condition. In their hands immediate manual replacement, combined with active anti-shock treatment, gave the best results. When reposition had to be delayed on account of shock or haemorrhage almost all the patients died.

SYMMETRICAL CORTICAL NECROSIS OF KIDNEYS.

Davis describes this condition occurring in a negress aged 24 in her first pregnancy: during the later pregnancy she had mild albuminuria, a raised blood-pressure and put on weight steadily. Near term a massive accidental haemorrhage occurred, for which Caesarean hysterectomy was performed. Suppression of urine, almost complete, followed the operation and persisted until death 10 days later.

Sections of the kidney showed infarcts due to the occlusion of small branches of the renal artery by organizing thrombi. The infarcted portion extended from medulla to capsule with the exception of a narrow subcapsular zone supplied by capsular vessels. All cellular details were lost. The arteries were occluded by masses of old fibrin, which was frequently replaced by young fibroblasts growing from the subendothelial tissue. In discussing the case and the general problem of cortical necrosis, Davis draws attention to this last finding in view of Gibberd's contention that symmetrical cortical necrosis may not be so uncommon, believing that for every fatal case a number occurs with less extensive involvement.

THE TREATMENT OF PREPUBERTIAL VULVO-VAGINITIS WITH A NEW SYNTHETIC OESTOGREN.

The material for this report consists of 25 cases of gonorrhoeal vulvovaginitis. The youngest child treated was 20 months and the oldest was 12 years of age.

On diagnosis of gonorrhoeal vulvo-vaginitis the child, irrespective of age, weight, duration of symptoms or previous therapy, was given a 1 mg. tablet of diethylstilboestrol three times a day until twenty had been taken. The tablet was crushed and administered in 2 ounces of milk. In 22 cases negative smears for pus and gonococci were obtained at the end of 7 days of treatment. Two cases required 9 days of treatment (27 mg.) and 18 days of treatment (54 mg.), respectively, to produce a cure.

Within 72 to 96 hours the discharge changes in character, becoming thin, mucoid and white. The latter type of discharge persists throughout treatment. The thick greenish yellow discharge definitely diminishes in amount within 36 to 48 hours.

In the first few cases treated some nausea and vomiting were noted, but these symptoms have not been observed since they have administered the drug in milk. They have observed 8 of these cases for 3 months after discontinuance of therapy and there have been no recurrences in any of them. Seven cases have been observed from 2 to 3 months.

TREATMENT OF NEPHROTIC OEDEMA.

These authors record a series of cases of nephrotic oedema. The main interest in their paper lies in the use of intravenous injection of solution of acacia. The patient is first put on a salt-free diet, and the diet contains a higher protein ration than is usually given, from 70 to 100 gm. per day. It is essential to provide extra vitamins for those patients who have been ill for a long time. The intake of fluid by mouth should be limited to about 800 c.c. per day.

Diuretic salts are usually prescribed in the form of potassium nitrate. Most patients receive 9 gm. daily, divided into three doses. The pills of potassium nitrate are better tolerated if taken with, or immediately after, meals. Enteric coated pills of 0.5 gm. each are used.

A 6 per cent solution of acacia in 0.06 per cent sodium chloride is used with advantage. It is best to begin the use of acacia 2 to 3 days after commencing the administration of potassium nitrate. The intravenous injection of a solution of acacia should take approximately one hour. It is advisable not to give more than 500 c.c. in one day and to repeat its administration on successive or alternate days until 90 or 120 gm., representing 3 or 4 injections, respectively, have been given. Most patients tolerate the injection without any untoward effects. The authors do not believe that, once its use is indicated, there exists any valid contra-indication to the administration of acacia except in the very rare case in which a severe allergic reaction to it has occurred. They have never seen evidence of renal damage attributable to the use of acacia nor have we observed instances in which the blood-pressure has remained at a higher level than that which existed previous to the injection.

Of 40 consecutive patients treated with acacia, 90 per cent could be dismissed from the hospital completely, or almost entirely, free from oedema.

The favourable effect of the administration of potassium nitrate is related definitely to its ability to increase the excretion of sodium chloride and water as well, and does not change significantly the colloid osmotic pressure of the serum.

THE USE OF DESOXYCORTICOSTERONE AND ITS ESTERS IN THE TREATMENT OF ADDISON'S DISEASE.

Gordon reviews the chemistry and clinical value of desoxycorticosterone. His conclusions are as follows:

(1) Of all the compounds which have been isolated from the adrenal cortex, desoxycorticosterone has the greatest action in conserving sodium and water and in causing the excretion of potassium.

(2) Of all the compounds studied, it has the least demonstrable action in maintaining normal carbohydrate metabolism in adrenal insufficiency, amounting practically to no effect in the clinical material studied.

(3) Given as the only form of replacement therapy in Addison's disease, it does not appear to provide complete substitution for the normal adrenal cortex.

Because of these considerations, it is highly probable that desoxycorticosterone does not represent the true hormone of the adrenal cortex but only one of the physiologically active sterols produced by that gland.

The deaths which have occurred incidental to the clinical use of desoxycorticosterone have probably been due for the most part to hypoglycaemia. The additional complications of oedema and hypertension have now been adequately controlled by means of reducing the intake of sodium salts to normal or even subnormal levels. Not only has it been found possible to allow normal quantities of potassium in the diet, but it has been found beneficial in some cases to administer extra potassium. Wilder and his associates believe that the dose of the hormone should not exceed 7 mg. and that the potassium intake should not be reduced below 4 gm. daily. This potassium intake can be conveniently provided by means of a high protein diet. Sodium salts are given sparingly.

P. MALPAS.

Revista de Obstetricia e Ginecologia de São Paula

Vol. iii, No. 6, April 1939.

Criminal abortion. Favero.

*Gigantic papilloma of the vulva. Godoy and Delascio.

*Painless parturition; the use of eupaco. Halasz.

Vol. iv, No. 1, June-August 1939.

*Investigation of the so-called capsule of uterine myomata. Amorim.

Some questions regarding neuro-endocrinology. De Moura Campos.

A Gigantic Papilloma of the Vulva.

The authors describe and illustrate by photographs and microphotographs a gigantic papilloma of the vulva. Originating as an apparently small wart, the tumour had been growing steadily for 8 years until it occupied almost the whole space between the labia. The patient, a multipara, came to hospital because it had become intensely painful and discharged freely.

Dismissing the hypothesis that such tumours are caused by a spirochete, though treponema are usually associated with them, the authors consider them due to a filtrable virus. Boujour's idea that the chief factor in producing papillomata or warts is mental agitation may be interesting, but is not quite satisfactory. Psychic suggestion may help to soothe the patient, but immediate removal is indicated. During pregnancy hormones seem to stimulate cell activity, but operation may be postponed till after term. In the case described the growth was removed by diathermy, and did not recur.

Though regarded as a benign epithelial new formation, the virus is infective and complications such as ulceration, haemorrhage, and even malignant change may occur.

Painless Parturition by using Eupaco Suppositories.

Halasz rapidly reviews the history of obstetric narcosis from ancient times when conditions of intoxication or hypnosis were induced, to more modern days when narcosis *à la Reine*, scopolamine, or barbiturates diminish maternal consciousness and pain, but are not always unattended by such accidents as uterine inertia, foetal asphyxia, or delay in placental detachment and haemorrhage. Halasz had satisfactory results with barbiturates in many cases, but in a few there had been placenta trouble.

Lately, he has employed eupaco suppositories, and describes 5 cases very successfully conducted. He hopes soon to record additional cases. Though at present observations are few he concludes that it is possible to obtain painless parturition by eupaco without hurt to either mother or child.

Eupaco is a combination of (*a*) eupaverin (an anti-spasmodic less toxic than papaverin), (*b*) methylbromide of atropin (acts on the nerve terminals of the para-sympathetic system), (*c*) luminal (hypnotic and sedative) and (*d*) dimethyl-phenazonum (analgesic). The synergic effect does not absolutely diminish the activity of the uterine contractions but they become painless. Three suppositories were usually given at intervals of about 1 hour according to the degree of cervical dilatation, and after rupture of the membranes. An injection of thymophysin was sometimes given. In some cases one suppository was sufficient.

Investigation of the so-called Capsule of Uterine Myomata.

Because of their great frequency, uterine myomata seem to be considered trivial rather uninteresting growths by both obstetricians and

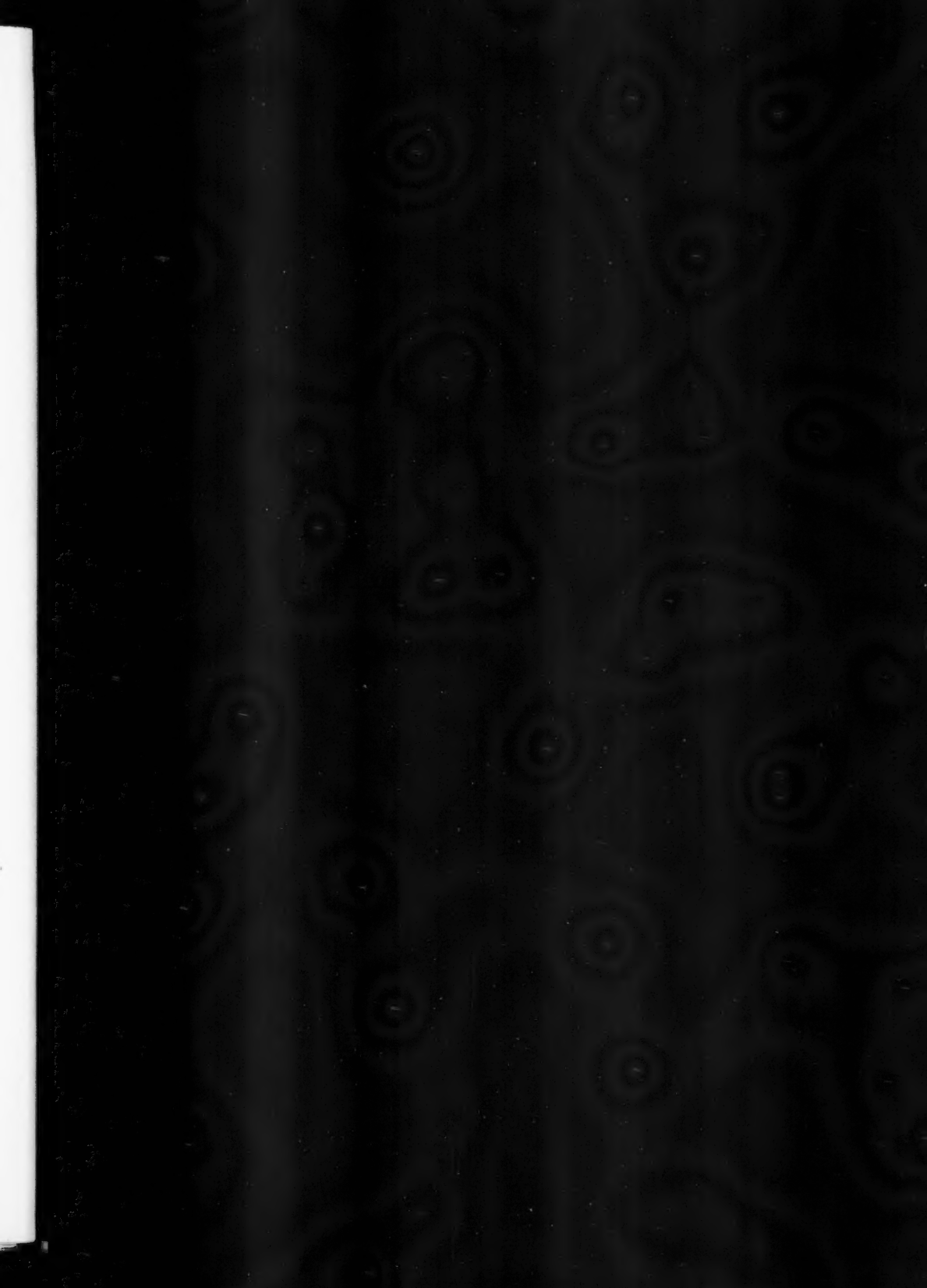
pathologists. Yet they possess a number of obscure points which furnish material for clinical and anatomico-pathological investigation.

Amorim reviews literature on the so-called capsule of uterine myomata, and gives his own clinical experience and histological investigation of many cases of uterine fibromyomata and their relation to uterine muscular tissue. The general opinion regarding these tumours is that they are distinctly encapsulated. Barbocci defined a fibromyoma as "a confluence of round nodules well circumscribed, and separated from neighbouring tissues by a conjunctive capsule". He thought this explained the ease with which they were enucleated.

Stern (1903) denied the existence of a capsule, and attributed the ease of separation to the contour's being divided by lamellae and fissures. The compression of surrounding tissues gave the concentric lamellae the appearance of a capsule, but between the so-called capsule and the uterine myometrium there is no clear limit. Amorim's descriptions and histological photographs lead him to the same conclusion as Stern.

To the naked eye, myomata show themselves limited by an area of myometrium in which fibres run concentrically parallel to a central axis. Under the microscope, they show no fibrous capsule, but a connexion with the axis of the tumour by fine fibres of smooth muscle. At the periphery the fibres become concentric and are divided by fissures covered with epithelium. Thus in a benign fibromyoma, there is parenchymatous continuity between the tumour and normal muscles of the uterine wall.

J. H. FILSHILL.



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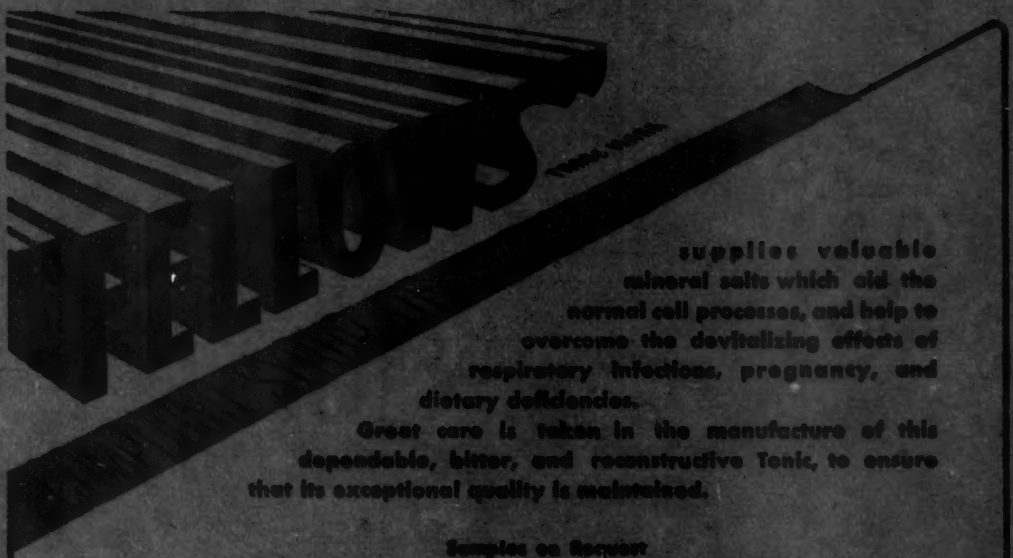

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